```
=> fil reg
FILE 'REGISTRY' ENTERED AT 14:47:34 ON 30 MAR 1999
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STRUCTURE FILE UPDATES:  26 MAR  99  HIGHEST RN 220764-97-6
DICTIONARY FILE UPDATES: 29 MAR  99  HIGHEST RN 220764-97-6

TSCA INFORMATION NOW CURRENT THROUGH JUNE 29, 1998

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> d stat que l15
L2                  SCR 1701
L6                  STR
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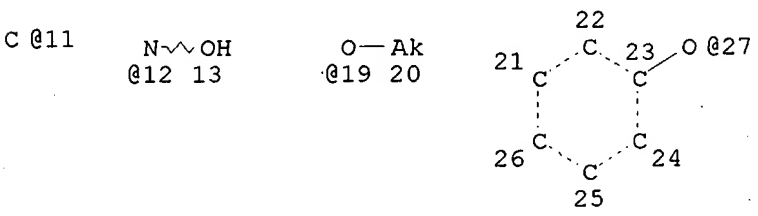

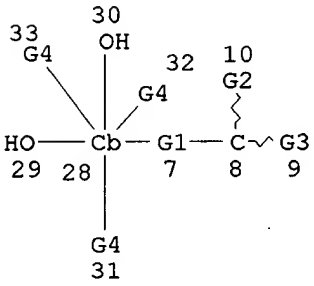


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VAR G3=NH2/12/19/27
VAR G4=H/OH
NODE ATTRIBUTES:
CONNECT IS M1  RC AT  11
DEFAULT MLEVEL IS ATOM
GGCAT   IS MCY  UNS  AT  28
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS X3 C  AT  20

GRAPH ATTRIBUTES:
RSPEC  21
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L8       1990951 SEA FILE=REGISTRY ABB=ON  PLU=ON  46.150.18/RID AND 1-2/NR NOT
                 (PMS/CI OR SQL/FA OR (S OR SI OR P)/ELS)
L9                SCR 2043 OR 2127 OR 1840 OR 2016 OR 2021 OR 2026
L11           183 SEA FILE=REGISTRY SUB=L8 CSS FUL L6 AND L2 NOT L9
L12           181 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11/COM
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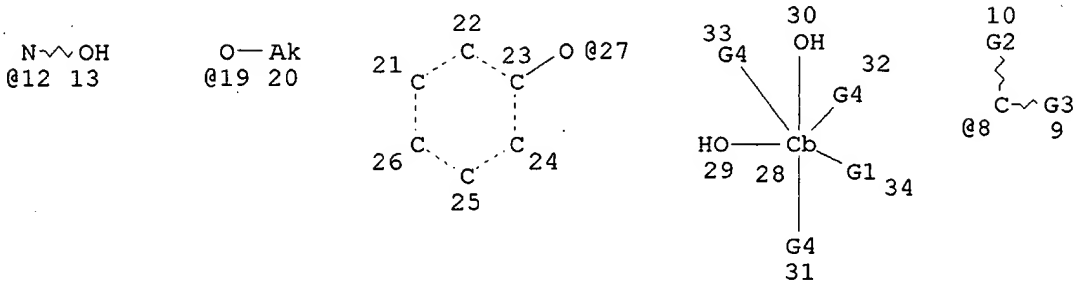
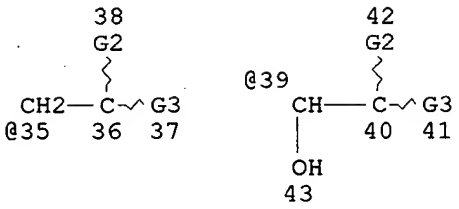
L13 STR





VAR G1=8/39/35
VAR G2=O/N/12
VAR G3=NH2/12/19/27
VAR G4=H/OH
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DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 28
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS X3 C AT 20

GRAPH ATTRIBUTES:
RSPEC 21
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE
L15 131 SEA FILE=REGISTRY SUB=L12 SSS FUL L13

100.0% PROCESSED 181 ITERATIONS 131 ANSWERS
SEARCH TIME: 00.00.03

=> d his l19-

(FILE 'REGISTRY' ENTERED AT 14:03:08 ON 30 MAR 1999)
E RIBONUCLEOTIDE REDUCTASE/CN
L19 3 S E3

FILE 'HCAPLUS' ENTERED AT 14:20:15 ON 30 MAR 1999
E ELFORD H/AU
L20 48 S E4-E6
L21 3178 S L15
L22 32 S L20 AND L21
L23 2414 S L19 OR RIBONUCLEOTIDE REDUCTASE
L24 43 S L21 AND L23
L25 5386 S (NF OR NUCLEAR FACTOR)(5A)KAPPA
L26 298 S (NF OR NUCLEAR FACTOR)(5A)KB
L27 155 S NFKB

all up for L15

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L28          478 S (NF OR NUCLEAR FACTOR)(5A)KAPPAB
L29         1468 S NFKAPPAB
L30            1 S NFBKAPPA
L31         5530 S L25-L30
L32            2 S L22 AND L31
L33            6 S L21 AND L31
L34            6 S L32,L33
                 E HEBVR
L35            9 S L21 AND ?DIABET?
L36           11 S L21 AND ?ARTERIOSCLER?
L37            0 S L21 AND ?ARTEROSCLER?
L38            0 S L21 AND ?ARTHEROSCLER?
L39            0 S L21 AND ?ARTHERIOSCLER?
L40           12 S L21 AND ?ATHEROSCLER?
L41            0 S L21 AND ?ATHERIOSCLER?
L42           11 S L21 AND ?TRANSPLANT?
L43          137 S L21 AND ?NEOPLAS?
L44          135 S L21 AND FREE RADICAL
L45           62 S L21 AND FREE RADICAL (L) SCAVENG?
L46          222 S L21 AND (?TUMOR? OR ?TUMOUR? OR ?MALIGN? OR ?CANCER? OR ?CARC
L47           29 S L43,L45,L46 AND L24
L48           22 S L43,L45,L46 AND L22
L49           67 S L34-L36,L40,L42,L47-L48
L50           10 S L22 NOT L49
L51            7 S L24 AND L50
L52           29 S L24 AND L49
L53           40 S L34,L51,L52
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:40:15 ON 30 MAR 1999
L54           39 S E1-E39
L55            1 S 69839-83-4
L56            1 S 95933-74-7
                 E N,3,4-TETRAHYDROXYBENZIMIDAMIDE/CN
L57            1 S 95933-72-5
                 E AMIDOX/CN
L58            1 S E3
L59            9 S 5/O AND L54
L60            3 S C7H7NO5 AND L59
L61            1 S 69839-82-3
L62            3 S L55,L56,L61

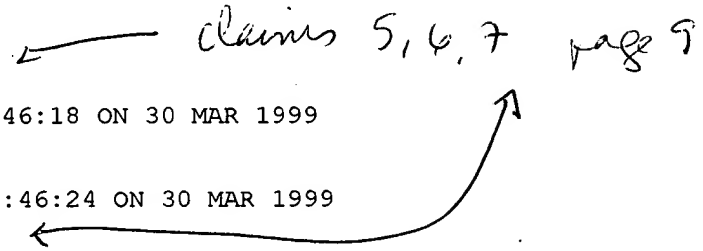
     FILE 'HCAOLD' ENTERED AT 14:46:18 ON 30 MAR 1999
L63            0 S L62

     FILE 'HCAPLUS' ENTERED AT 14:46:24 ON 30 MAR 1999
L64           64 S L62
L65           36 S L64 AND L53
L66            4 S L53 NOT L65
L67            3 S L66 NOT 18/SC,SX
L68           39 S L65,L67

     FILE 'REGISTRY' ENTERED AT 14:47:34 ON 30 MAR 1999

=> d ide can tot l19

L19  ANSWER 1 OF 3  REGISTRY  COPYRIGHT 1999 ACS
RN   9068-66-0  REGISTRY
CN   Reductase, ribonucleoside triphosphate (9CI)  (CA INDEX NAME)
```



OTHER NAMES:
CN 5'-Deoxyadenosylcobalamin-dependent ribonucleoside triphosphate reductase
CN Anaerobic ribonucleotide reductase
CN Class II ribonucleotide reductase
CN Class III ribonucleotide reductase
CN E.C. 1.17.4.2
CN Ribonucleoside triphosphate reductase
CN **Ribonucleotide reductase**
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CABA, CAPLUS, CIN, EMBASE, PROMT, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
138 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
138 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:179229

REFERENCE 2: 130:164766

REFERENCE 3: 130:62711

REFERENCE 4: 130:35462

REFERENCE 5: 129:327713

REFERENCE 6: 129:287249

REFERENCE 7: 129:256746

REFERENCE 8: 129:170142

REFERENCE 9: 129:146155

REFERENCE 10: 129:109304

L19 ANSWER 2 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN 9047-64-7 REGISTRY
CN Reductase, ribonucleoside diphosphate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ADP reductase
CN CDP reductase
CN Class I ribonucleotide reductase
CN E.C. 1.17.4.1
CN NrdEF enzyme
CN Nucleoside diphosphate reductase
CN Ribonucleoside 5'-diphosphate reductase
CN Ribonucleoside diphosphate reductase
CN Ribonucleotide diphosphate reductase
CN **Ribonucleotide reductase**
CN UDP reductase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CABA, CAPLUS, CIN, CSCHEM, EMBASE, PROMT, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

905 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
905 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182286

REFERENCE 2: 130:150263

REFERENCE 3: 130:139629

REFERENCE 4: 130:134895

REFERENCE 5: 130:121377

REFERENCE 6: 130:106913

REFERENCE 7: 130:106903

REFERENCE 8: 130:106843

REFERENCE 9: 130:91205

REFERENCE 10: 130:90199

L19 ANSWER 3 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN 9040-57-7 REGISTRY
CN Reductase, ribonucleotide (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Deoxyribonucleotide reductase
CN **Ribonucleotide reductase**
CN RNA reductase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, EMBASE, NIOSHTIC, PROMT, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
803 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
803 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:179221

REFERENCE 2: 130:178357

REFERENCE 3: 130:177527

REFERENCE 4: 130:150274

REFERENCE 5: 130:150162

REFERENCE 6: 130:147747

REFERENCE 7: 130:136628

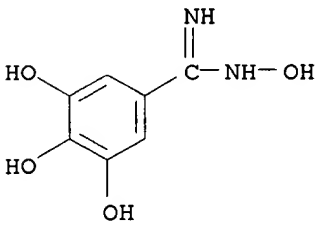
REFERENCE 8: 130:135671

REFERENCE 9: 130:134946

REFERENCE 10: 130:119145

=> d ide can tot l62

L62 ANSWER 1 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN **95933-74-7** REGISTRY
CN Benzenecarboximidamide, N,3,4,5-tetrahydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN N,3,4,5-Tetrahydroxybenzimidamide
CN Trimidox
FS 3D CONCORD
MF C7 H8 N2 O4
CI COM
LC STN Files: ADISINSIGHT, BIOBUSINESS, BIOSIS, CA, CAPLUS, IPA, PHAR, PROMT, TOXLINE, TOXLIT, USPATFULL



20 REFERENCES IN FILE CA (1967 TO DATE)
20 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:177527

REFERENCE 2: 129:310457

REFERENCE 3: 129:211378

REFERENCE 4: 129:170304

REFERENCE 5: 129:156586

REFERENCE 6: 128:136198

REFERENCE 7: 128:123476

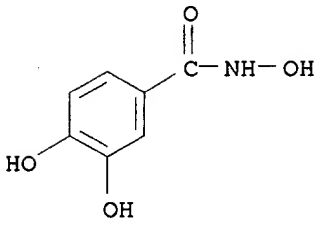
REFERENCE 8: 127:243220

REFERENCE 9: 127:185517

REFERENCE 10: 127:130355

L62 ANSWER 2 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN **69839-83-4** REGISTRY
CN Benzamide, N,3,4-trihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3,4-Dihydroxybenzohydroxamic acid
CN 3,4-Dihydroxyphenylhydroxamic acid
CN Didox
CN N,3,4-Trihydroxybenzamide
CN NSC 324360

CN VF 147
FS 3D CONCORD
DR 106573-41-5
MF C7 H7 N O4
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CIN, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



47 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
47 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:177527

REFERENCE 2: 129:311381

REFERENCE 3: 129:310528

REFERENCE 4: 129:310457

REFERENCE 5: 129:156586

REFERENCE 6: 128:149556

REFERENCE 7: 128:123476

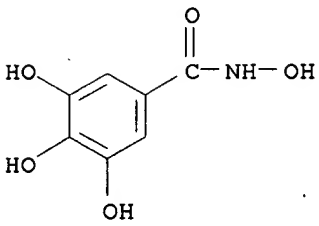
REFERENCE 8: 128:31747

REFERENCE 9: 127:243220

REFERENCE 10: 127:185517

L62 ANSWER 3 OF 3 REGISTRY COPYRIGHT 1999 ACS
RN **69839-82-3** REGISTRY
CN Benzamide, N,3,4,5-tetrahydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3,4,5-Trihydroxybenzohydroxamic acid
CN 3,4,5-Trihydroxyphenylhydroxamic acid
CN Gallohydroxamic acid
CN NSC 324362
CN VF 122
FS 3D CONCORD
DR 106554-64-7
MF C7 H7 N O5
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS, DDFU, DRUGU,

EMBASE, MEDLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



25 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
25 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:220280

REFERENCE 2: 125:33284

REFERENCE 3: 124:254237

REFERENCE 4: 122:230109

REFERENCE 5: 120:26122

REFERENCE 6: 109:162929

REFERENCE 7: 106:60880

REFERENCE 8: 105:108095

REFERENCE 9: 105:75714

REFERENCE 10: 104:199673

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:48:27 ON 30 MAR 1999
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FILE COVERS 1967 - 30 Mar 1999 VOL 130 ISS 14
FILE LAST UPDATED: 30 Mar 1999 (19990330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGistRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d bib abs hitrn tot l68

L68 ANSWER 1 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1999:113524 HCAPLUS
DN 130:177527
TI Therapeutic process for inhibiting **NF-.kappa.B**
IN **Elford, Howard L.**
PA USA
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906009	A2	19990211	WO 98-US15715	19980729

PI W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 97-54230 19970730
AB A therapeutic process is provided for the inhibition of **NF-.kappa.B** in mammals in whose cells **NF-.kappa.B** has been activated by an agency external to said cell.
IT **9040-57-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; therapeutic process for inhibiting **NF-.kappa.B**)
IT **69839-83-4**, N,3,4-Trihydroxybenzamide **95933-72-5**, Amidox **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic process for inhibiting **NF-.kappa.B**)

L68 ANSWER 2 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:601960 HCAPLUS
DN 129:310457
TI Antimalarial activities of polyhydroxyphenyl and hydroxamic acid derivatives
AU Holland, Kevin P.; **Elford, Howard L.**; Bracchi, Valerie; Annis, Charles G.; Schuster, Sheldon M.; Chakrabarti, Debopam
CS Interdisciplinary Center for Biotechnology Research, University of Florida, Gainesville, FL, 32611, USA
SO Antimicrob. Agents Chemother. (1998), 42(9), 2456-2458
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Several known mammalian **ribonucleotide reductase** inhibitors featuring a polyhydroxyphenyl and/or hydroxamate moiety as the active group were screened for potency in inhibiting growth of the malaria parasite Plasmodium falciparum. Compds. contg. a 2,3- or 3,4-dihydroxyphenyl group as well as benzohydroxamate appear to be the most effective inhibitors of the malaria parasite.
IT **16053-97-7 69839-83-4**, VF 147 **95933-72-5 95933-74-7 214692-31-6**, VF 268
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimalarial activities of polyhydroxyphenyl and hydroxamic acid

derivs.)
IT **9040-57-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; antimalarial activities of polyhydroxyphenyl and hydroxamic acid derivs.)

L68 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:569457 HCAPLUS
DN 129:310528
TI Iron binding capacity of didox (3,4 dihydroxybenzohydroxamic acid) and amidox (3,4 dihydroxybenzamidoxime) two inhibitors of the enzyme **ribonucleotide reductase**
AU Fritzer-Szekeres, Monika; Novotny, Ladislav; Vachalkova, Anna; Gobl, Rainer; **Elford, Howard L.**; Szekeres, Thomas
CS Clinical Institute of Medical and Chemical Laboratory Diagnostics, Univ. Vienna, Vienna, 1090, Austria
SO Adv. Exp. Med. Biol. (1998), 431(Purine and Pyrimidine Metabolism in Man IX, 1998), 599-604
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Publishing Corp.
DT Journal
LA English
AB **Ribonucleotide reductase** is the rate-limiting enzyme of deoxynucleoside triphosphate synthesis and is an excellent target for **cancer** chemotherapy. Didox and amidox inhibit this enzyme and have in vitro and in vivo **antitumor** activity. The ability of didox and amidox to interfere with the iron metab. was studied by photometric and polarog. methods. Didox and amidox formed iron complexes. Their cytotoxic action could not be circumvented by the addn. of Fe ammonium citrate, indicating that the iron complexing capacity is not responsible for the mechanism of their action. When L1210 leukemia cells were incubated with the didox-iron or amidox-iron complex itself, only slight changes of the 50% growth inhibitory capacity of the complex in comparison with didox or amidox alone was seen. Thus, didox and amidox can form iron complexes, but in contrast to other agents, their **anticancer** activity cannot be contributed to this effect alone.
IT **69839-83-4**, Didox **95933-72-5**, Amidox
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(iron binding capacity of didox and amidox as inhibitors of **ribonucleotide reductase** and **antitumor** activity)

L68 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:487631 HCAPLUS
DN 129:211378
TI Enhanced effects of Adriamycin by combination with a new **ribonucleotide reductase** inhibitor, trimidox, in murine leukemia
AU Fritzer-Szekeres, Monika; Novotny, Ladislav; Romanova, Darina; Gobl, Rainer; Sedlak, Jan; Vachalkova, Anna; Rauko, Peter; **Elford, Howard L.**; Szekeres, Thomas
CS Clinical Institute for Medical and Chemical Laboratory Diagnostics, Vienna, A-1090, Austria
SO Life Sci. (1998), 63(7), 545-552
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English

AB **Ribonucleotide reductase** is the rate limiting enzyme of de novo DNA synthesis; its activity is significantly increased in **tumor** cells related to the proliferation rate. Therefore the enzyme is considered to be an excellent target for **cancer** chemotherapy. In the present study we tested the in vitro and in vivo **antitumor** effects of a drug combination using trimidox (3,4,5-trihydroxybenzamidoxime), a novel inhibitor of **ribonucleotide reductase** with adriamycin, a widely used **anticancer** drug. This combination was selected because adriamycin generates **free radicals** being responsible for cardiotoxic side effects, trimidox has been shown to be a good **free radical scavenger**. The in vitro cytotoxic effect of the drug combination was examd. in L1210 mouse leukemia cells employing a MTT chemosensitivity assay. Incubation of these cells with adriamycin and trimidox together yielded less than additive cytotoxic effects compared to either drug alone. These effects were not caused by the involvement of p-glycoprotein mediated drug efflux. However, when the effect of trimidox and adriamycin in combination was examd. in L1210 leukemia bearing mice **antitumor** effects of adriamycin could be enhanced by the presence of trimidox. Our data indicate, that the in vivo combination of adriamycin together with trimidox might be beneficial for the treatment of **malignancies**.

IT **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced effects of Adriamycin by combination with a new **ribonucleotide reductase** inhibitor, trimidox, in murine leukemia)

IT **9040-57-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhanced effects of Adriamycin by combination with a new **ribonucleotide reductase** inhibitor, trimidox, in murine leukemia)

L68 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:429154 HCAPLUS
DN 129:170304
TI Trimidox-mediated morphological changes during erythroid differentiation is associated with the stimulation of hemoglobin and F-cell production in human K562 cells
AU Iyamu, Efe W.; Adunyah, Samuel E.; **Elford, Howard L.**; Fasold, Hugo; Turner, Ernest A.
CS Comprehensive Sickle Cell Center, Nashville, TN, 37208, USA
SO Biochem. Biophys. Res. Commun. (1998), 247(3), 759-764
CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB Trimidox (3,4,5-trihydroxybenzamidoxime) has been shown to reduce the activity of **ribonucleotide reductase** with accompanied growth inhibition and differentiation of mammalian cells. Hydroxyurea (HU) is the only **ribonucleotide reductase** inhibitor in clin. use for the treatment and management of sickle cell anemia, since this compd. increases fetal Hb (Hb F) prodn.: a potent inhibitor of sickle Hb (Hb,SS) polymn. However, the main limitations of HU is its lack of potency, myelosuppression and short half life. These studies investigated the effects of trimidox on the induction of Hb and F-cells prodn. in K562 erythroleukemia cells. Our study reveals that trimidox exhibits concn. dependent inhibitory effect on K562 cells with increase in benzidine pos.

normoblasts and F-cells prodn. as well as morphol. changes typical of erythroid differentiation. These findings provide the first evidence that the growth inhibitory differentiation of cells induced by trimidox enhance Hb and F-cells prodn. (c) 1998 Academic Press.

IT **95933-74-7**, Trimidox
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trimidox-mediated morphol. changes during erythroid differentiation is assocd. with the stimulation of Hb and F-cell prodn. in human K562 cells)

IT **9040-57-7, Ribonucleotide reductase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(trimidox-mediated morphol. changes during erythroid differentiation is assocd. with the stimulation of Hb and F-cell prodn. in human K562 cells)

L68 ANSWER 6 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:415518 HCAPLUS
DN 129:156586
TI Interaction of gallium nitrate with other inhibitors of **ribonucleotide reductase**: effects on the proliferation of human leukemic cells
AU Myette, Michael S.; **Elford, Howard L.**; Chitambar, Christopher R.
CS Division of Hematology/Oncology, Medical College of Wisconsin, Milwaukee, WI, 53226, USA
SO Cancer Lett. (Shannon, Irel.) (1998), 129(2), 199-204
CODEN: CALEDQ; ISSN: 0304-3835
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB **Ribonucleotide reductase**, a key enzyme in deoxyribonucleotide synthesis, is an important target for **cancer** chemotherapy. Drugs that inhibit its individual components may act synergistically to block DNA synthesis. Prior work has established that gallium inhibits the R2 subunit of **ribonucleotide reductase**. We show that gallium acts synergistically with the **ribonucleotide reductase** inhibitors gemcitabine and hydroxyurea to inhibit the proliferation of CCRF-CEM cells. In contrast, combinations of gallium with the **ribonucleotide reductase** inhibitors amidox, didox, or trimidox produced antagonistic effects on cell growth. Spectroscopy anal. revealed that as a result of their metal-binding properties, amidox, didox and trimidox formed complexes with gallium, thus negating potential synergistic actions. Our results have important implications in the design of clin. trials using these **ribonucleotide reductase** inhibitors in combination.

IT **69839-83-4**, Didox **95933-72-5**, Amidox **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interaction of gallium nitrate with other inhibitors of **ribonucleotide reductase** and effects on proliferation of human leukemic cells)

IT **9040-57-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interaction of gallium nitrate with other inhibitors of **ribonucleotide reductase** and effects on proliferation of human leukemic cells)

L68 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:49701 HCAPLUS
DN 128:149556
TI DNA-protective activity of new **ribonucleotide reductase** inhibitors
AU Rauko, Peter; Romanova, Darina; Miadokova, Eva; Macakova, Kvetoslava; Novotny, Ladislav; **Elford, Howard L.**; Szekeres, Thomas
CS Department of Experimental Therapy, Cancer Research Institute, Slovak Academy of Sciences, Bratislava, SK-8123Z, Slovakia
SO Anticancer Res. (1997), 17(5A), 3437-3440
CODEN: ANTRD4; ISSN: 0250-7005
PB Anticancer Research
DT Journal
LA English
AB The DNA-protective activity of hydroxyurea (HU) and novel **ribonucleotide reductase** (RR) inhibitors amidox (AX), didox (DX) and trimidox (TX) was examd. using hydrogen peroxide as the DNA-damaging agent. The exposure of superspiralized plasmid DNA mols. (pBR 322) to H2O2 under precisely defined in vitro conditions initiates a change in DNA topol. (DNA form I relaxes to DNA form II). This electrophoretically monitored change in the plasmid DNA topol. is related to the induction of ss-DNA breaks and corresponds with DNA exposition to **free radicals**. The inhibition of DNA relaxation (the prevention of DNA damage induced by hydrogen peroxide) depended on the **free radical scavenging** capacity of the drugs investigated. HU exerted DNA protective activity at a concn. of 4 mM, AX at concn. of 1 .mu.M, TX at a concn. of 5 .mu.M and DX at a concn. of 25 .mu.M (the **free radical scavenging** activity increases from HU to AX in following manner: HU .mchlt. DX < TX < AX). It can be concluded that the new synthetic RR-inhibitor AX which is being investigated at the preclin. level as a potential anti-**cancer** drug possess the highest capacity for **scavenging** of **free radicals**.
IT **69839-83-4**, Didox **95933-72-5**, Amidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA-protective activity of new **ribonucleotide reductase** inhibitors and hydroxyurea in relation to radical scavenging capacity)
IT **9040-57-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; DNA-protective activity of new **ribonucleotide reductase** inhibitors and hydroxyurea in relation to radical scavenging capacity)

L68 ANSWER 8 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:26676 HCAPLUS
DN 128:136198
TI Enhanced effects of adriamycin by combination with a new **ribonucleotide reductase** inhibitor, trimidox, in murine leukemia
AU Novotny, L.; Romanova, D.; Gobl, R.; Sedlak, J.; Vachalkova, A.; Rauko, P.; Fritzer-Szekeres, M.; **Elford, H. L.**; Szekeres, T.
CS Cancer Research Inst., SAS, Bratislava, SK-812 32, Slovakia
SO Haematol. Blood Transfus. (1998), 39(Acute Leukemias VII), 556-561
CODEN: HBTRDV; ISSN: 0171-7111
PB Springer-Verlag
DT Journal

LA English
AB **Ribonucleotide reductase** is the rate limiting enzyme of de novo DNA synthesis; its activity is significantly increased in **tumor** cells related to the proliferation rate of the **tumor** cell. Therefore the enzyme is considered to be an excellent target for **cancer** chemotherapy. In the present study we tested the in vitro and in vivo **antitumor** effects of a drug combination using trimidox (3,4,5-trihydroxybenzohydroxamidoxime), a novel inhibitor of **ribonucleotide reductase** with adriamycin, a widely used **anticancer** drug. This combination was selected because adriamycin generates **free radicals**, which are responsible for cardiotoxic side effects of adriamycin treatment, and because trimidox has been shown to be a good **free radical scavenger** . The in vitro cytotoxic effect of the drug combination was examd. in L 1210 mouse leukemia cells employing an MTT chemo-sensitivity assay. Simultaneous in vitro incubation of these cells yielded antagonistic cytotoxic effects compared to either drug alone. These effects were not caused by the involvement of p-glycoprotein mediated drug efflux. However, when the effect of trimidox and adriamycin in combination was examd. in L 1210 leukemia bearing mice, **antitumor** effects of adriamycin could be enhanced by the presence of trimidox. Animals were treated on day two after **tumor** cell injection with 5 mg/kg adriamycin and received 250 mg/kg trimidox on days 2,3 and 4. Mice treated with adriamycin or trimidox alone yielded a 41 and 38% increase in life span, resp. However, animals, which were treated with both drugs, showed a 89% increase of their life span. Our data indicate, that in vitro results of drug combinations should be interpreted with extreme caution and suggest that the in vivo combination of adriamycin together with trimidox might be beneficial for the treatment of **malignancies.**
IT **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adriamycin antileukemic effects enhancement by **ribonucleotide reductase** inhibitor trimidox)

L68 ANSWER 9 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:795554 HCAPLUS
DN 128:123476
TI Effective use of **ribonucleotide reductase** inhibitors (didox and trimidox) alone or in combination with didanosine (ddI) to suppress disease progression and increase survival in murine acquired immunodeficiency syndrome (MAIDS)
AU Mayhew, Christopher; Oakley, Oliver; Piper, James; Hughes, Nedda K.; Phillips, Jonathan; Birch, Nicholas J.; **Elford, Howard L.**; Gallicchio, Vincent S.
CS Laboratory of Experimental Immunohematopoiesis and Developmental Therapeutics, Departments of Clinical Sciences and Internal Medicine, Chandler Medical Center, University of Kentucky, Lexington, KY, 40536, USA
SO Cell. Mol. Biol. (Paris) (1997), 43(7), 1019-1029
CODEN: CMOBEF; ISSN: 0145-5680
PB C.M.B. Association
DT Journal
LA English
AB **Ribonucleotide reductase** inhibitors (RRIs) have been recently shown to inhibit retroviral replication. We examd. a new series of RRIs, 3,4-dihydroxybenzohydroxamic acid (Didox) and 3,4,5-trihydroxybenzohydroxamidoxime (Trimidox) for their ability to alter disease progression in murine acquired immunodeficiency syndrome (MAIDS),

both alone and in combination with 2',3'-dideoxyinosine (ddI). MAIDS disease was induced by inoculation of female C57BL/6 mice with the LP-BM5 murine leukemia virus (MuLV) and disease progression characterized by extensive peripheral lymphadenopathy and splenomegaly. Efficacy of treatment with these drugs was based upon their ability to influence survival and disease pathophysiol. by monitoring the development of splenomegaly. Toxicity was detd. by changes in body wt., total peripheral white blood cell count and hematocrit. Didox or trimidox monotherapy was assocd. with increased survival and decreased disease pathophysiol., with no apparent toxicity. Combined with ddI, their ability to reduce development of viral induced splenomegaly was enhanced compared to trimidox, didox or ddI alone. These results demonstrate RRIs have potent activity in reversing the disease manifestations characteristic of MAIDS. Further studies are warranted to det. human clin. efficacy.

IT **9040-57-7**, **Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **ribonucleotide reductase** inhibitors (didox and trimidox) alone or in combination with didanosine: suppression of MAIDS)

IT **69839-83-4**, Didox **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ribonucleotide reductase** inhibitors (didox and trimidox) alone or in combination with didanosine: suppression of MAIDS)

L68 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:713810 HCAPLUS
DN 128:31747
TI Iron binding capacity of DIDOX (3,4-dihydroxybenzohydroxamic acid) and AMIDOX (3,4-dihydroxybenzamidoxime) new inhibitors of the enzyme **ribonucleotide reductase**
AU Fritzer-Szekeres, Monika; Novotny, Ladislav; Vachalkova, Anna; Findenig, Gabriele; **Elford, Howard L.**; Szekeres, Thomas
CS Clinical Institute for Medical and Chemical Laboratory Diagnostics, University of Vienna, Vienna, 1090, Austria
SO Life Sci. (1997), 61(22), 2231-2237
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier
DT Journal
LA English
AB **Ribonucleotide reductase** is the rate limiting enzyme of deoxynucleoside triphosphate synthesis and is considered to be an excellent target of **cancer** chemotherapy. Didox and amidox are newly synthesized compds., which inhibit this enzyme and have in vitro and in vivo **antitumor** activity. We have now investigated the capability of didox and amidox to interfere with the iron metab. We show by photometric and polarog. methods, that didox and amidox are capable of forming an iron complex. However, their cytotoxic action cannot be completely circumvented by addn. of Fe-ammoniumcitrate, indicating that the iron complexing capacity may not be responsible for the mechanism of action of these compds. When L1210 leukemia cells were incubated with the didox-iron or amidox-iron complex itself, changes of the 50% growth inhibitory capacity of the complex in comparison with didox or amidox alone could be shown. We conclude, that didox and amidox are capable of forming iron complexes, but in contrast to other agents, the **anticancer** activity cannot be contributed to this effect alone. Future studies will have to elucidate the mol. mechanism of action of these new and promising **anticancer** agents.

IT **69839-83-4**, DIDOX **95933-72-5**, AMIDOX
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iron binding capacity of DIDOX (3,4-dihydroxybenzohydroxamic acid) and AMIDOX (3,4-dihydroxybenzamidoxime) new inhibitors of the enzyme **ribonucleotide reductase**)
IT **9040-57-7, Ribonucleotide reductase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(iron binding capacity of DIDOX (3,4-dihydroxybenzohydroxamic acid) and AMIDOX (3,4-dihydroxybenzamidoxime) new inhibitors of the enzyme **ribonucleotide reductase**)

L68 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:655454 HCAPLUS
DN 127:298548
TI Dermatologic preparation
IN Murase, Takatoshi; Hase, Tadashi; Tokimitsu, Ichiro
PA Kao Corporation, Japan; Murase, Takatoshi; Hase, Tadashi; Tokimitsu, Ichiro
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9735618	A1	19971002	WO 97-JP488	19970221
	W: CN, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	JP 09255547	A2	19970930	JP 96-66077	19960322
PRAI	JP 96-66077		19960322		

AB A dermatol. prepn. contg. an **NF.kappa**.B activation inhibitor and usable for preventing or ameliorating epidermolysis, pachymenia, skin chopping, disorder of skin texture, pigmentation, degeneration or breakdown of corium constituents, and pruritus, thus being useful for various skin troubles.
IT **99-24-1**, Methyl gallate **121-79-9**, Propyl gallate **831-61-8**, Ethyl gallate **1138-60-9**, Isopropyl gallate
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dermatol. prepn. contg. **NF.kappa**.B activation inhibitor)

L68 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:567538 HCAPLUS
DN 127:243220
TI Selective inhibition of I.kappa.B.alpha. phosphorylation and HIV-1 LTR-directed gene expression by novel antioxidant compounds
AU Lee, Raymond; Beauparlant, Pierre; **Elford, Howard**; Ponka, Premysl; Hiscott, John
CS Lady Davis Institute for Medical Research, McGill University, Montreal, PQ, H3T 1E2, Can.
SO Virology (1997), 234(2), 277-290
CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB Oxidative stress activates the **NF-.kappa**.B/Rel transcription factors which are involved in the activation of numerous

immunoregulatory genes and the human immunodeficiency virus type 1 (HIV-1) long terminal repeat (LTR). In the present study, we examd. the effects of established and novel compds. including antioxidants, **ribonucleotide reductase** inhibitors, and iron chelators on **NF-.kappa.**B activation and HIV LTR-mediated gene expression induced by TNF-.alpha.. N-Acetylcysteine (NAC), pyrrolidinedithiocarbamate (PDTC), and Trimidox (TD) at various concns. inhibited TNF-.alpha.-induced **NF-.kappa.**B binding in Jurkat cells. Pretreatment of cells with these compds. prior to stimulation prevented I.kappa.B.alpha. degrdn. Phosphorylation of I.kappa.B.alpha., a prerequisite for its signal-induced degrdn., was abrogated in these cells, indicating that oxidative stress is an essential step in the **NF-.kappa.**B activation pathway. On the other hand, iron chelators desferrioxamine, pyridoxal isonicotinoyl hydrazone (PIH), and salicylaldehyde isonicotinoyl hydrazone (SIH) showed no inhibition of TNF-.alpha.-induced **NF-.kappa.**B DNA-binding activity. Synergistic induction of HIV-1 LTR-mediated gene expression by TNF-.alpha. and the HIV-1 transactivator Tat in Jurkat cells was significantly suppressed in the presence of NAC and TD, but not PDTC. The inhibition of NAC and TD on LTR-directed gene expression was diminished when **NF-.kappa.**B-binding sites in the LTR were deleted, indicating that these compds. affected the **NF-.kappa.**B component of the synergism. Iron chelators PIH and SIH also showed some inhibitory effect on LTR-mediated gene activation, presumably through an **NF-.kappa.**B-independent mechanism. These expts. demonstrate that TD, at concn. 50 times lower than the effective concn. of NAC, potently inhibits **NF-.kappa.**B activity and suppresses HIV LTR expression.

IT **69839-83-4**, Didox **95933-72-5**, Amidox **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(inhibition of I.kappa.B.alpha. phosphorylation and HIV-1 LTR-directed gene expression by antioxidants)

L68 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:529356 HCAPLUS
DN 127:130355
TI The effect of new combinations of antimetabolites and trimidox on **cancer** cells
AU Romanova, D.; Raslova, H.; Plaschke, K.; Novotny, L.; Fritzer, M.
CS Ustav experimentalnej onkologie, Bratislava, 812 32, Slovakia
SO Farm. Obz. (1995), 64(7-8), 180-187
CODEN: FAOBAS; ISSN: 0014-8172
PB Zdravotnicke Vydavatelstvo HERBA
DT Journal; General Review
LA Slovak
AB A review with 22 refs. The effects of trimidox, a new inhibitor of **ribonucleotide reductase**, used in combination with antimetabolites arabinosylcytosine (ara-C) and gemcitabine (difluorodideoxycytidine) used in **anticancer** chemotherapy were studied in vitro cultures of human colon **cancer** HT-29 cells. The effects trimidox were compared with the effects of thiazofurine combined with hypoxanthine or allopurinol. The cytostatic effects were also evaluated in human leukemic cells HL-60. The levels of ribonucleoside and deoxyribonucleoside triphosphates and cell cycle responses were detd. The mechanisms of trimidox action, biochem. pathways, **anticancer** activity, synergism, and cytotoxicity are discussed.

IT **69839-83-4**, Didox **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antitumor** effect of trimidox in combination of antimetabolites in **cancer** cells)

L68 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:499818 HCAPLUS
DN 127:185517
TI Genotoxic properties of the newly synthesized **antineoplastic** agents amidox, didox, and trimidox
AU Miadokova, E.; Macakova, K.; Podstavkova, S.; Vlcek, D.
CS Department Genetics, Faculty Sciences, Bratislava, 84215, Slovakia
SO Pharmazie (1997), 52(7), 540-544
CODEN: PHARAT; ISSN: 0031-7144
PB Govi-Verlag Pharmazeutischer Verlag
DT Journal
LA English
AB Toxic and genotoxic effects of 3 polyhydroxy-substituted benzohydroxamates (amidox, didox, and trimidox), having **antineoplastic** activities by the mechanism of the **ribonucleotide reductase** activity inhibition, were evaluated by reverse mutation assay on Salmonella typhimurium strains TA97, TA98, TA100, TA102. While amidox did not exert any toxic effect, didox, and trimidox were toxic. The toxicity of the test chems. was dependent on the structure of their mol. and the repair capacity of the test strains. Trimidox exhibited the highest toxicity, and it was proved as a direct-acting frameshift mutagen. Its mutagenic effect was increased after a metabolic activation. Amidox and didox can be classified as frameshift promutagens.
IT **69839-83-4**, Didox **95933-72-5**, Amidox **95933-74-7**, Trimidox
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genotoxicity of **antineoplastic** agents)
IT **9047-64-7**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(genotoxicity of **antineoplastic** agents amidox, didox, and trimidox caused by inhibition of)

L68 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:327317 HCAPLUS
DN 127:39615
TI The new inhibitors of **ribonucleotide reductase**. Comparison of some physicochemical properties
AU Romanova, Darina; Vachalkova, Anna; Szekeres, Thomas; **Elford, Howard L.**; Novotny, Ladislav
CS Cancer Res. Inst. Slovak Academy Sci., Bratislava, SK-81232, Slovakia
SO J. Pharm. Biomed. Anal. (1997), 15(7), 951-956
CODEN: JPBADA; ISSN: 0731-7085
PB Elsevier
DT Journal
LA English
AB Amidox (AX), didox (DX) and trimidox (TX), compds. synthesized as new **ribonucleotide reductase** inhibitors, have been investigated by UV spectrophotometry, polarog. HPLC. The expts. were performed at various pH values. The changes in UV absorption of the compds. studied were recorded and it was demonstrated that these changes are related to the pH and to structural features of the investigated mols. Only amidox and trimidox were reduced during polarog. expts. in

Britton-Robinson buffer. The redn. of both compds. proceeded in 2 1-electron steps in acid solns. One 2-electron diffuse irreversible wave was obsd. at basic pH values. The values of the half-wave potential became more neg. with increasing pH values. HPLC assay also showed changes in the retention of compds. investigated, particularly when the pH of the mobile phase was close to the dissocn. const. of the particular drug. The changes of physicochem. properties detected by the methods are related to different chem. structures (the most significant changes were obsd. in alk. pH).

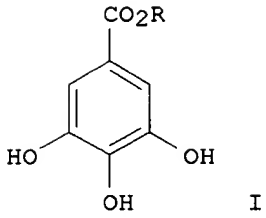
IT **9040-57-7**, **Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(physicochem. properties of **ribonucleotide reductase** inhibitors)

IT **69839-83-4**, Didox **95933-72-5**, Amidox **95933-74-7**
, Trimidox
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(physicochem. properties of **ribonucleotide reductase** inhibitors)

L68 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:315140 HCAPLUS
DN 126:288106
TI **NF-.kappa.**B activation inhibitors, antiviral agents, and immunosuppressants containing gallic acid derivatives
IN Murase, Takatoshi; Hase, Tadashi; Tokimitsu, Ichiro
PA Kao Corp, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09059151	A2	19970304	JP 95-215983	19950824

OS MARPAT 126:288106
GI



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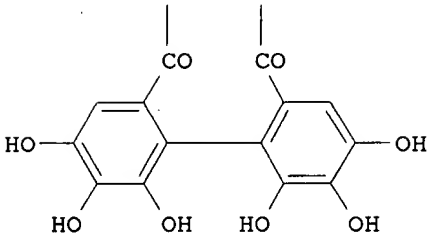


AB The **NF-.kappa.B** activation inhibitors and the antiviral agents contain .gtoreq.1 selected from gallic acid esters I [R = C1-24 linear or branched (hydroxy)alkyl, (hydroxy)alkenyl], (b) tannins contg. galloyl group, and (c) tannins having hexahydroxydiphenoyl group Q as active ingredients. Immunosuppressants contg. (b) and/or (c) as active ingredients are also claimed. The inhibitors are useful for treatment of infections with viruses, e.g. HIV, HTLV-I, CMV, and adenovirus, whose transcription is promoted by **NF-.kappa.B**. Octyl gallate showed 65% inhibition against IL-1.alpha.-stimulated activation of **NF-.kappa.B** in cultured vascular epithelial cells. Formulations contg. gallate esters or 1,2,3,6-tetragalloylglucose are also given.

IT **99-24-1**, Methyl gallate **121-79-9**, Propyl gallate **831-61-8**, Ethyl gallate **1138-60-9**, Isopropyl gallate
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**NF-.kappa.B** activation inhibitors, antiviral agents, and immunosuppressants contg. gallic acid esters or tannins)

L68 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:1007365 HCAPLUS
DN 124:75813
TI Iron binding capacity of trimidox (3,4,5-trihydroxybenzamidoxime), a new inhibitor of the enzyme **ribonucleotide reductase**
AU Szekeres, Thomas; Vielnascher, Elisabeth; Novotny, Ladislav; Vachalkova, Anna; Fritzer, Monika; Findenig, Gabriele; Goebl, Rainer; **Elford, Howard L.**; Goldenberg, Hans
CS Inst. Medizinsche Chemie, Univ. Wien, Vienna, Austria
SO Eur. J. Clin. Chem. Clin. Biochem. (1995), 33(11), 785-9
CODEN: EJCBEO; ISSN: 0939-4974
DT Journal
LA English
AB **Ribonucleotide reductase** is the rate limiting enzyme of deoxynucleoside triphosphate synthesis and is considered to be an excellent target of **cancer** chemotherapy. Trimidox, a newly

synthesized compd., inhibits this enzyme and has in vitro and in vivo **antitumor** activity. As trimidox was able to upregulate the expression of the transferrin receptor in HL-60 human promyelocytic leukemia cells, the authors have now investigated the capability of trimidox to interfere with iron metab. The authors show by photometric and polarog. methods that trimidox is able to form an iron complex. However, its cytotoxic action cannot be circumvented by addn. of iron-satd. transferrin or iron-ammonium citrate, indicating that the iron complexing capacity is not responsible for the mechanism of action of this compd. When HL-60, K562 or L1210 leukemia cells were incubated with the trimidox-iron complex itself, the authors could observe increases of the 50% growth inhibitory capacity of the complex in comparison with trimidox alone. The authors conclude that trimidox is able to form an iron complex, but in contrast to other agents, the **anticancer** activity cannot be contributed to this effect alone. Further studies will have to elucidate the mol. mechanism of action of this new and promising **anticancer** agent.

IT **9068-66-0, Ribonucleotide reductase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitor; iron binding capacity of trimidox (3,4,5-trihydroxybenzamidoxime), a new inhibitor of the enzyme **ribonucleotide reductase**)

IT **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iron binding capacity of trimidox (3,4,5-trihydroxybenzamidoxime), a new inhibitor of the enzyme **ribonucleotide reductase**)

L68 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:982076 HCAPLUS
DN 124:134431
TI **Ribonucleotide reductase** as target for enzyme-directed chemotherapy. Effects of trimidox (3,4,5-trihydroxybenzohydroxamidoxime), a new inhibitor of **ribonucleotide reductase**
AU Findenig, G.; Vielnascher, E.; Goebl, R.; Fritzer-Szekeres, M.; Szekeres, T.
CS Inst. Med. Chem., Univ. Wien, Vienna, A-1090, Austria
SO Wien. Klin. Wochenschr. (1995), 107(22), 694-7
CODEN: WKWOAO; ISSN: 0043-5325
DT Journal; General Review
LA German
AB A review with 28 refs. describing the biochem., morphol., and cytotoxic effects of trimidox and other polyhydroxy-substituted benzohydroxamate derivs. on leukemia cell lines. Selection criteria, effects, and combinations used in enzyme-targeted chemotherapy are described for these **ribonucleotide reductase** inhibitors.

IT **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ribonucleotide reductase** as target for enzyme-directed chemotherapy)

IT **9047-64-7, Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ribonucleotide reductase** as target for enzyme-directed chemotherapy)

L68 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:732741 HCAPLUS

DN 123:188481
TI **NF-.kappa.B** transcription factor activation by hydrogen peroxide can be decreased by 2,3-dihydroxybenzoic acid and its ethyl ester derivative
AU Sappey, Christine; Boelaert, Johan R.; Legrand-Poels, Sylvie; Grady, Robert W.; Piette, Jacques
CS Lab. Virol., Univ. Liege, Liege, B-4000, Belg.
SO Arch. Biochem. Biophys. (1995), 321(1), 263-70
CODEN: ABBIA4; ISSN: 0003-9861
DT Journal
LA English
AB Reactive oxygen species like hydrogen peroxide (H2O2) have been shown to serve as messengers in the induction of **NF-.kappa.B** and, hence, in the activation and replication of human immunodeficiency virus type 1 (HIV-1) in human cells. Several antioxidant compds. and iron chelators have been shown to interfere with both **NF-.kappa.B** and HIV-1 activation under oxidative stress. Because 2,3-dihydroxybenzoic acid (DHB) and its Et ester deriv. (DHB-EE) are potent oral iron chelators, the authors started to investigate their effects on monocytes treated with increasing H2O2 concns. These two compds. exert important protective effects against the cytotoxic effect of H2O2 as 300 .mu.M DHB or DHB-EE increased cell survival from 30 to 85%. The treatment of monocytes with increasing amts. of H2O2 (from 0 to 3 mM) leads to the nuclear induction of **NF-.kappa.B** which is dose dependently inhibited by both DHB and DHB-EE. Addn. of ferric ions to DHB only partially restores the **NF-.kappa.B** induction by H2O2, while this effect is almost completely restored by ferric ion addn. to DHB-EE. Using spin trapping coupled to ESR, the authors have demonstrated that DHB and, to a lesser extent, DHB-EE trapped hydroxyl radicals produced by H2O2 photolysis. These data demonstrate that small arom. mols. harboring both iron-chelating and antioxidant properties like DHB and DHB-EE can effectively interfere with the deleterious effects of H2O2 in monocytes where iron overload can be obsd. in HIV-1-infected patients.
IT **3943-73-5**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**NF-.kappa.B** transcription factor activation by hydrogen peroxide can be decreased by 2,3-dihydroxybenzoic acid and its Et ester deriv. in relation to cytoprotective activity in monocytes and HIV-1 virus infection treatment)

L68 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:270272 HCAPLUS
DN 122:45904
TI Synergistic growth inhibitory and differentiating effects of trimidox and tiazofurin in human promyelocytic leukemia HL-60 cells
AU Szekeres, Thomas; Fritzer, Monika; Strobl, Herbert; Gharehbaghi, Kamran; Findenig, Gabriele; **Elford, Howard L.**; Lhotka, Christian; Schoen, Hans J.; Jayaram, Hiremagalur N.
CS Inst. Med. Chem., Univ. Vienna Med. Sch., Vienna, Austria
SO Blood (1994), 84(12), 4316-21
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
AB Increased **ribonucleotide reductase** (RR) activity has been linked with **malignant** transformation and **tumor** cell growth. Therefore, this enzyme is considered to be an excellent target for **cancer** chemotherapy. The authors have examd. the

effects of a newly patented RR inhibitor, trimidox (3,4,5-trihydroxybenzohydroxamidoxime). Trimidox inhibited the growth of human promyelocytic leukemia HL-60 cells with an IC50 of 35 .mu.mol/L. Incubation of HL-60 cells with 50 .mu.mol/L trimidox for 24 h decreased deoxyguanosine triphosphate (dGTP) and deoxycytidine triphosphate (dCTP) pools to 24% and 39% of control values, resp. Incubation of HL-60 cells with 20 to 80 .mu.mol/L trimidox even up to a period of 4 days did not alter the distribution of cells in different phases of cell cycle. Sequential incubation of HL-60 cells with trimidox (25 .mu.mol/L) for 24 h and then with 10 .mu.mol/L tiazofurin (an inhibitor of inosine monophosphate dehydrogenase) for 4 days produced synergistic growth inhibitory activity, and the cell no. decreased to 16% of untreated controls. When differentiation-linked cell surface marker expressions were detd. in cells treated with trimidox and tiazofurin, a significantly increased fluorescence intensity was obsd. for the CD 11b (2.9-fold), CD 33 (1.9-fold), and HLA-D cell surface antigens. Expression of the transferrin receptor (CD71) increased 7.3-fold in cells treated with both agents, compared with untreated controls. The results suggest that trimidox in combination with tiazofurin might be useful in the treatment of leukemia.

IT **95933-74-7**, Trimidox
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic growth inhibitory and differentiating effects of trimidox and tiazofurin in human promyelocytic leukemia HL-60 cells)

IT **9040-57-7**, **Ribonucleotide reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synergistic growth inhibitory and differentiating effects of trimidox and tiazofurin in human promyelocytic leukemia HL-60 cells)

L68 ANSWER 21 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:225331 HCAPLUS
DN 122:230109
TI Relationship of **antitumor** activity and the electronic structure of **ribonucleotide reductase** inhibitors
AU Luo, Y. F.; Xu, X.; Liang, Y.; Cai, W. Z.
CS Dep. Natural Drug, Sun YatSen Univ. Med. Sci., Canton, 510089, Peop. Rep. China
SO Yaoxue Xuebao (1994), 29(9), 673-9
CODEN: YHHPAL; ISSN: 0513-4870
DT Journal
LA Chinese
AB By using the CNDO/2 quantum chem. method, 32 substituted hydroxamic acids, 6 substituted benzamides and 9 substituted Me benzoates have been calcd. Among them 44 compds. were studied by step regression method. Two quant. structure-(ribonucleotidfe resuctase inhibitory) activity relationships of two groups (hydroxamic acids and benzamides, Me benzoates) were obtained. They were (1) PC = 3.00-2.27 CQS-0.15 EHOMO + 0.22 SHEP for substituted hydroxamic acids and (2) PC = 10.06-0.96 CQS + 1.07 E LUMO + 0.66 SHEP for substituted benzamides and Me benzoates. The results show that the quantum chem. indexes in the two QSAR affected the inhibitory activity to similar degree and the mechanism of inhibition. of **ribonucleotide reductase** by inhibitors involves metal chelation. Furthermore, the effects of the structure of 35 compds. on the life span of L1210 leukemia-bearing mice were studied by pattern recognition method. The **antitumor** activity classification figure obtained by four parameters .pi., CQS, ELUMO and SHEP, is satisfactory. This indicates that the **antitumor** activities of these compds. are the result of inhibiting ribonucleotide resuctase which is governed by the speed of

these compds. to reach the acceptors.

IT **9040-57-7, Ribonucleotide reductase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; relationship of **antitumor** activity and electronic structure of **ribonucleotide reductase** inhibitors)

IT **99-24-1**, Methyl 3,4,5-trihydroxybenzoate **618-73-5**, 3,4,5-Trihydroxybenzamide **2150-43-8**, Methyl 3,4-dihydroxybenzoate **2150-44-9**, Methyl 3,5-dihydroxybenzoate **2150-45-0**, Methyl 2,6-dihydroxybenzoate **2150-46-1**, Methyl 2,5-dihydroxybenzoate **2150-47-2**, Methyl 2,4-dihydroxybenzoate **2411-83-8**, Methyl 2,3-dihydroxybenzoate **16053-97-7**, 2,3-Dihydroxybenzohydroxamic acid **22372-31-2**, 2,3,4-Trihydroxybenzohydroxamic acid **27286-93-7**, 2,5-Dihydroxybenzohydroxamic acid **30697-84-8**, 3,5-Dihydroxybenzohydroxamic acid **35318-15-1**, 2,4-Dihydroxybenzohydroxamic acid **35318-17-3**, 2,6-Dihydroxybenzohydroxamic acid **54337-90-5**, 3,4-Dihydroxybenzamide **56128-66-6**, Methyl 2,3,4-trihydroxybenzoate **69839-82-3**, 3,4,5-Trihydroxybenzohydroxamic acid **69839-83-4**, 3,4-Dihydroxybenzohydroxamic acid **70022-11-6**, 2,3,4-Trihydroxybenzamide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(relationship of **antitumor** activity and electronic structure of **ribonucleotide reductase** inhibitors)

L68 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:569910 HCAPLUS
DN 121:169910
TI Biochemical and **antitumor** activity of trimidox, a new inhibitor of **ribonucleotide reductase**
AU Szekeres, Thomas; Gharehbaghi, Kamran; Fritzer, Monika; Woody, Michael; Srivastava, Arun; van't Riet, Bart; Jayaram, Hiremagalur N.; **Elford, Howard L.**
CS Inst. Med. Chem., Univ. Vienna, Austria
SO Cancer Chemother. Pharmacol. (1994), 34(1), 63-6
CODEN: CCPHDZ; ISSN: 0344-5704
DT Journal
LA English
AB Trimidox (3,4,5-trihydroxybenzamidoxime), a newly synthesized analog of didox (N,3,4-trihydroxybenzamide) reduced the activity of **ribonucleotide reductase** (EC 1.17.4.1) in exts. of L1210 cells with an IC50 of 5 .mu.M, whereas hydroxyurea, the only **ribonucleotide reductase** inhibitor in clin. use, exhibited an IC50 of 500 .mu.M. **Ribonucleotide reductase** activity was also measured in situ by incubating L1210 cells for 24 h with trimidox at 7.5 .mu.M (a concn. that inhibited cell proliferation by 50%) or at 100 .mu.M for 2 h; these concns. resulted in a decrease in enzyme activity to 22% and 50%, resp., of the control value. Trimidox and hydroxyurea were cytotoxic to L1210 cells, with IC50 values of 7.5 and 50 .mu.M, resp. Vs. **ribonucleotide reductase**, trimidox and hydroxyurea had IC50 values of 12 and 87 .mu.M, resp. Trimidox concn.-dependently increased the life span of mice bearing L1210 leukemia. The **antitumor** activity appeared more pronounced in female mice than in male mice. These findings suggest that trimidox is a new and potent inhibitor of **ribonucleotide reductase** and that it is a promising candidate for the chemotherapy of **cancer** in humans.

IT **69839-83-4**, Didox **95933-74-7**, Trimidox
RL: BIOL (Biological study)
(**ribonucleotide reductase**- and **neoplasm**
-inhibiting activities of)
IT **9040-57-7**
RL: BIOL (Biological study)
(trimidox inhibition of, **neoplasm** inhibition in relation to)

L68 ANSWER 23 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:315474 HCAPLUS
DN 120:315474
TI transgenic mouse model of pharmacologic induction of fetal hemoglobin: studies using a new **ribonucleotide reductase** inhibitor, Didox
AU Pace, B.S.; **Elford, H.L.**; Stamatoyannopoulos, G.
CS Dep. Med., Univ. Washington, Seattle, WA, 98195, USA
SO Am. J. Hematol. (1994), 45(2), 136-41
CODEN: AJHEDD; ISSN: 0361-8609
DT Journal
LA English
AB Evaluation of pharmacol. agents that stimulate fetal Hb prodn. has been done mainly in baboons and macaques. The authors investigated whether results in transgenic mice can predict the stimulation of fetal Hb in primates, by testing .gamma. globin induction in response to a new **ribonucleotide reductase** inhibitor, Didox. A transgenic mouse line carrying the human A.gamma. gene linked to a locus control region cassette was used. Treatment of transgenic mice with Didox resulted in induction of .gamma. gene expression as documented by an increase in F reticulocytes and F cells and an elevation of .gamma./.gamma. + .beta. biosynthetic ratio. Similarly, administration of Didox to a baboon in the nonanemic and chronically anemic state resulted in induction of .gamma. gene expression as shown by increases in F reticulocytes, F cells, and Hb F. These results suggest that the .mu.LCR-A.gamma. transgenic mice can be used to screen new pharmacol. compds. for .gamma. globin inducibility.
IT **69839-83-4**, Didox
RL: BIOL (Biological study)
(Hb F formation induction by, .mu.LCR-A.gamma. transgenic mice as model for screening of drugs for fetal Hb induction in relation to)

L68 ANSWER 24 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:420495 HCAPLUS
DN 119:20495
TI Benzamidoximes for treatment of diseases involving excess free-radical formation
IN van't Riet, Bartholomeus; **Elford, Howard L.**; Wampler, Galen L.
PA USA
SO U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 302,946, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

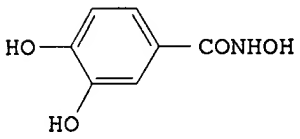
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5183828	A	19930202	US 90-555834	19900720
	US 4623659	A	19861118	US 83-497370	19830523
	US 4942253	A	19900717	US 86-907562	19860915
PRAI	US 83-497370	19830523			
	US 86-907562	19860915			

US 89-302946 19890130
OS MARPAT 119:20495
AB Hydroxy-substituted benzamidoximes are prepd. as **ribonucleotide reductase** inhibitors and **free radical scavengers**. Thus, 3,4-dihydroxybenzamidonitrile was reacted with hydroxylamine sulfate which had been neutralized by NaOH and stirred at 45.degree. for 18 h to obtain 3,4-dihydroxybenzamidoxime (I), which was reacted with HCl to obtain I.cntdot.HCl (II). **Free-radical scavenging** ability of II was in vitro tested.
IT **9040-57-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, polyhydroxybenzoic acid derivs. as)
IT **95933-83-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of)
IT **95933-72-5P 95933-74-7P 95933-79-2P 95933-80-5P 97186-79-3P 147510-60-9P 147510-61-0P 147510-62-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **ribonucleotide reductase** inhibitor and **free radical scavenger**)
IT **70022-11-6**, 2,3,4-Trihydroxybenzamide
RL: RCT (Reactant)
(reaction of, with phosphorous oxychloride)

L68 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:524102 HCAPLUS
DN 117:124102
TI Studies on the mechanisms of inhibition of L1210 cell growth by 3,4-dihydroxybenzohydroxamic acid and 3,4-dihydroxybenzamidoxime
AU Tihan, Tarik; **Elford, Howard L.**; Cory, Joseph G.
CS Coll. Med., Univ. South Florida, Tampa, FL, 33612, USA
SO Adv. Enzyme Regul. (1991), 31, 71-83
CODEN: AEZRA2; ISSN: 0065-2571
DT Journal
LA English
AB Didox and Amidox inhibit L1210 cell growth in culture. At least one of the mechanism in the mode(s) of action of the compds. is directed at the **ribonucleotide reductase** site. Partially purified prepns. of **ribonucleotide reductase** activity are inhibited by Amidox and Didox. The formation of deoxycytidine nucleotides from [14C]cytidine in intact L1210 cells is also blocked. Didox and Amidos cause the decrease in the intracellular pools of the 4 dNTPs. Hydroxyurea-resistant L1210 cells are not cross-resistant to either Didox or Amidox. These data suggest that Didox and Amidox are not inhibiting **ribonucleotide reductase** through a mechanism similar to hydroxyurea.
IT **69839-83-4**, Didox **95933-72-5**, Amidox
RL: PRP (Properties)
(cytotoxicity of, **ribonucleotide reductase** inhibition in)
IT **9047-64-7**
RL: PROC (Process)
(inhibition of, by Amidox and Didox, cytotoxicity in relation to)

L68 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1988:562838 HCAPLUS
DN 109:162838
TI A phase 1 and pharmacokinetic study of didox: a **ribonucleotide**

reductase inhibitor
AU Veale, D.; Carmichael, J.; Cantwell, B. M. J.; **Elford, H. L.**; Blackie, R.; Kerr, D. J.; Kaye, S. B.; Harris, A. L.
CS Reg. Cardiothorac. Cent., Freeman Hosp., Newcastle-upon-Tyne, NE7 7DN, UK
SO Br. J. Cancer (1988), 58(1), 70-2
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
GI



I

AB A phase 1 study of a new **ribonucleotide reductase** inhibitor didox (I) was performed by administration of escalating doses of the drug by slow i.v. injection. Patients with unresponsive **metastatic carcinoma** received the drug. There were 13 escalations of dosage, from a starting dose of 192 mg/m2 to 10 g/m2.. Dose-limiting toxicity was encountered at 7.5 g/m2, where disturbances of hepatic and renal function were obsd., in addn. to severe gastrointestinal toxicity. Pharmacokinetic studies showed that a peak level of I was achieved within 5 min of injection. At 1,728 mg/m2 the data best fitted a 2-compartment open model, with mean absorption and elimination half-lives of 5.2 and 41.3 min, resp. Less than 10% of the drug was excreted unchanged in the urine, and the majority of this excretion was within 6 h. Didox can therefore be safely given by slow i.v. injection at 6 g/m2.
IT **69839-83-4**, Didox
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pharmacokinetics and toxicity of, in humans)

L68 ANSWER 27 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1987:60880 HCAPLUS
DN 106:60880
TI Biomolecular dynamics and electron spin resonance spectra of copper complexes on **antitumor** agents in solution
AU Basosi, R.; Trabalzini, L.; Pogni, R.; Antholine, W. E.
CS Dep. Chem., Univ. Siena, Siena, 53100, Italy
SO J. Chem. Soc., Faraday Trans. 1 (1987), 83(1), 151-9
CODEN: JCFTAR; ISSN: 0300-9599
DT Journal
LA English
AB For the purpose of developing new **antitumor** agents which are more efficacious and have less generalized toxicity than existing ones, the free-radical generation and metal complexation of well known **anticancer** agents have been studied. Copper(II) ion complexes are readily formed with several members of a class of hydroxyurea derivs. which are known to be effective **ribonucleotide reductase** inhibitors. E.s.r. measurements and u.v.-visible titrn. illustrate weak binding for 3,4-dihydroxybenzohydroxamic acid and tight binding in complex formation for gallohydroxamic acid and 2,3,4-trihydroxybenzohydroxamic acid. These data were used in a preliminary investigation of cytotoxicity, and the results are consistent with single phase cell cycle killing.

IT **22372-31-2 69839-82-3 69839-83-4**
RL: FORM (Formation, nonpreparative)
(formation of, cytotoxic mechanism in relation to)
IT **22372-31-2DP**, iron complexes **69839-82-3DP**, iron complexes **69839-83-4DP**, iron complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L68 ANSWER 28 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1986:508095 HCAPLUS
DN 105:108095
TI Lycurim in combination chemotherapy with acivicin or 3,4,5-trihydroxybenzohydroxamic acid in vitro
AU Ban, Jasna; Olah, Edith; Van't Riet, Bart; Weber, George
CS Lab. Exp. Cancerol., Cent. Inst. Tumors Allied Dis., Zagreb, 41000, Yugoslavia
SO Period. Biol. (1986), 88(1), 19-24
CODEN: PDBIAD; ISSN: 0031-5362
DT Journal
LA English
AB Possible synergism in the cytotoxic activity of the alkylating agent, lycurim [4148-16-7], in combination with 2 different antimetabolites, acivicin [42228-92-2], an inhibitor of glutamine-utilizing enzymes, and3,4,5-trihydroxybenzohydroxamic acid (VF 122) [**69839-82-3**], an inhibitor of **ribonucleotide reductase** was studied. Expts. were performed on proliferating rat hepatoma 3924A cells in tissue culture. Lycurim together with VF 122 resulted in synergistic killing in hepatoma cells treated for 7 days, as detd. by its colony-forming ability. Synergism was also obsd. when hepatoma cells were treated with both lycurim and acivicin for 7 days. Thus, lycurim is an effective drug for inducing synergistic cytotoxicity with the 2 antimetabolites acivicin or VF 122.
IT **69839-82-3**
RL: BIOL (Biological study)
(cytotoxicity of acivicin and, synergism in)

L68 ANSWER 29 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1986:199673 HCAPLUS
DN 104:199673
TI Potentiation of antimetabolite action by dibromodulcitol in cell culture
AU Olah, Edith; Kremmer, Tibor; Boldizsar, Marianne
CS Res. Inst. Oncopathol., Natl. Inst. Oncol., Budapest, H-1122, Hung.
SO Adv. Enzyme Regul. (1985), 24, 155-75
CODEN: AEZRA2; ISSN: 0065-2571
DT Journal
LA English
AB Acivicin [42228-92-2], pyrazofurin [30868-30-5], tiazofurin [60084-10-8] and VF-122 [**69839-82-3**] were lethal against 3924A hepatoma cells in the exponential phase of growth with IC50 of 1.5, 5, 10 and 4.5 .mu.M, resp. All these antimetabolites exhibited cytotoxicity preponderantly against exponential-phase cultures, indicating that all the 4 drugs belong to Class II (phase-specific agents) in the Kinetic Classification of **Anticancer** Agents (Bruce, W. R. et al., 1966). Dibromodulcitol (I) [10318-26-0] a bifunctional alkylating agent, revealed cycle-specific cytotoxicity (Class III agent) against hepatoma 3924A, yielding IC50 values of 2.3 and 5.5 .mu.M for exponentially and stationary growing cells, resp. Synergistic interaction was obsd. when I in combination with acivicin, pyrazofurin and tiazofurin was examd. I in combination with VF-122 exhibited additive lethality against hepatoma

cells in culture. The synergistic and additive cytotoxicity in combinations of I with these antimetabolites was accompanied by the concurrent depletion of ribonucleotide and(or) deoxyribonucleotide pools. The synergistic biol. results of drug combinations of acivicin with I can be accounted for by the action of acivicin in inhibiting CTP synthetase [9023-56-7], resulting in a synergistic decrease in CTP [65-47-4] content, and by inhibition of DNA synthesis caused by I. The synergistic and additive depletion of UTP [63-39-8], CTP, dTTP [365-08-2], and dCTP [2056-98-6] pools in the combination of I the pyrazofurin may be responsible for the synergistic lethality of these combinations. Synergism, in terms of pool depletion, was obsd. for GTP [86-01-1] and dCTP; summation was detected for dGTP [2564-35-4] when I and tiazofurin were given concurrently. The synergistic cytotoxicity of this drug combination may be a consequence of these alterations. The additive lethality of I-VF-122 drug combination was reflected in the additive elevations of the ribonucleoside diphosphate concns. Apparently, treatments based on the Kinetic Classification and on the biochem. targeting of the drug should have an impact on the design of in vivo chemotherapy.

IT **9047-64-7**
RL: BIOL (Biological study)
(dibromodulcitol potentiation of antimetabolites **neoplasm** inhibition in relation to)

IT **69839-82-3**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**neoplasm**-inhibiting activity of, dibromodulcitol potentiation of, biochem. mechanism of)

L68 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1985:166480 HCAPLUS
DN 102:166480
TI Polyhydroxybenzoic acid derivatives
IN Van't Riet, Bartholomeus; Wampler, Galen L.; **Elford, Howard L.**
PA USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8404676	A1	19841206	WO 84-US755	19840521
	W: AU, DK, FI, JP, NO, SU				
	RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
	US 4623659	A	19861118	US 83-497370	19830523
	AU 8430130	A1	19841218	AU 84-30130	19840521
	AU 589111	B2	19891005		
	EP 144396	A1	19850619	EP 84-902270	19840521
	EP 144396	B1	19910102		
	R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
	JP 60501409	T2	19850829	JP 84-502128	19840521
	JP 05001780	B4	19930111		
	AT 59553	E	19910115	AT 84-902270	19840521
	CA 1339221	A1	19970805	CA 84-454910	19840523
	NO 8403739	A	19841206	NO 84-3739	19840919
	FI 8403681	A	19841124	FI 84-3681	19840920
	DK 8500137	A	19850111	DK 85-137	19850111
	JP 05078299	A2	19930330	JP 92-39794	19920226

PRAI US 83-497370 19830523
EP 84-902270 19840521
WO 84-US755 19840521

AB (HO)nC6H5-n(CHR)mCR1:NR2(R, R2 = H, OH, R1 = alkoxy, NH2, NHOH; n = 2-5; m = 0, 1) were prepd. Thus, 3,4,5-(HO)3C6H2CONH2 was refluxed in EtOAc with SOCl2 to give 86% 3,4,5-(HO)3C6H2CN. This was stirred with H2NOH.H2SO4 at 45.degree. in H2O contg. NaOH and Na2SO3, then acidified to give 80% 3,4,5-(HO)3C6H2C(:NOH)NH2.HCl (I). I is an inhibitor of **ribonucleotide reductase** with an IC50 of 5.mu.M and 59mg I/kg i.p. in mice infected with L-1210 leukemia cells increased survival time 90.0%.

IT **618-73-5 70022-11-6**
RL: RCT (Reactant)
(dehydration of)

IT **9040-57-7**
RL: PROC (Process)
(inhibition of, by polyhydroxybenzamidine derivs.)

IT **618-73-5P 95933-72-5P 95933-74-7P 95933-79-2P 95933-80-5P 97186-79-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and **antitumor** activity of)

IT **95933-83-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L68 ANSWER 31 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1984:472459 HCAPLUS
DN 101:72459
TI Hydroxybenzohydroxamic acids, benzamides and esters and related compounds as **ribonucleotide reductase** inhibitors
IN Van't Riet, Bartholomeus; **Elford, Howard L.**; Wampler, Galen L.
PA USA
SO U.S., 7 pp. Cont.-in-part U.S. 4,394,389.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4448730	A	19840515	US 82-370023	19820420
	US 4263322	A	19810421	US 79-16472	19790301
	US 4394389	A	19830719	US 81-247171	19810324

PRAI US 79-16472 19790301
US 81-247171 19810324

AB The title compds. were prepd. which showed **ribonucleotide reductase** inhibiting activity and **antitumor** activity (extensive data given). Thus, 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, 3,5-dihydroxy-, and 2,3,4-, and 3,4,5-trihydroxybenzohydroxamic acids were prepd. by treating the corresponding Me polyhydroxybenzoates with NH2OH.H2SO4 in aq. NaOH soln.

IT **9040-57-7**
RL: RCT (Reactant)
(inhibitors of, hydroxybenzohydroxamic acids and related compds.)

IT **25379-88-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with hydroxylamine sulfate)

IT **16053-97-7P 22372-31-2P 27286-93-7P**

30697-84-8P 35318-15-1P 35318-17-3P
69839-82-3P 69839-83-4P 70022-13-8P
91362-81-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

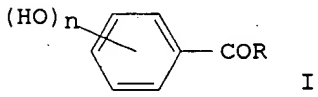
IT **99-24-1 2150-43-8 2150-44-9 2150-45-0**
2150-46-1 2150-47-2 2411-83-8
56128-66-6
RL: RCT (Reactant)
(reaction of, with hydroxylamine sulfate)

IT **618-73-5 54337-90-5 70022-11-6**
RL: RCT (Reactant)
(**ribonucleotide reductase** inhibition and leukemia inhibition by)

L68 ANSWER 32 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1983:569526 HCAPLUS
DN 99:169526
TI Hydroxybenzohydroxamic acids, benzamides and esters as **ribonucleotide reductase** inhibitors
IN Van't Riet, Bartholomeus; **Elford, Howard L.**; Wampler, Galen L.
PA USA
SO U.S., 6 pp. Cont.-in-part of U.S. 4,263,322.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4394389	A	19830719	US 81-247171	19810324
	US 4263322	A	19810421	US 79-16472	19790301
	US 4448730	A	19840515	US 82-370023	19820420
PRAI	US 79-16472	19790301			
	US 81-247171	19810324			

GI



I

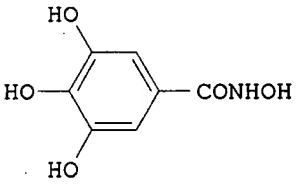
AB The title compds. (I; R = NH2, NHOH, NH(C1-C3) alkyl, aryl-NH, N[(C1-C3)alkyl]2, or OPh; n = 2 or 3) inhibit **ribonucleotide reductase** [**9040-57-7**] and, thus are useful as **neoplasm** inhibitors, esp. against leukemias. Thus, 2,3,4-trihydroxybenzohydroxamic acid [**22372-31-2**] was prepd., as a potent reductase inhibitor, and when given to mice bearing various **neoplasms**, inhibited **tumor** growth and increased longevity.

IT **9040-57-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, hydroxybenzohydroxamic acids and hydroxybenzamides as, **neoplasm** inhibition in relation to)

IT **618-73-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and and **ribonucleotide reductase**-inhibiting and **neoplasm**-inhibiting activity of)

IT **16053-97-7P 22372-31-2P 27286-93-7P**
30697-84-8P 35318-15-1P 35318-17-3P
54337-90-5P 69839-82-3P 69839-83-4P
70022-11-6P 70022-13-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **ribonucleotide reductase**-inhibiting and **neoplasm**-inhibiting activity of)
IT **2150-45-0P 56128-66-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L68 ANSWER 33 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1983:256 HCAPLUS
DN 98:256
TI Cytotoxic and cell kinetic effects of 3,4,5-trihydroxybenzohydroxamic acid (VF 122) in hepatoma 3924A cells
AU Ban, Jasna; Olah, Edith; Weber, George
CS Sch. Med., Indiana Univ., Indianapolis, IN, 46223, USA
SO Cancer Treat. Rep. (1982), 66(12), 2071-80
CODEN: CTRRDO; ISSN: 0361-5960
DT Journal
LA English
GI

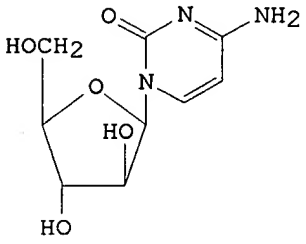


I

AB VF 122 (I) [**69839-82-3**], an inhibitor of **ribonucleotide reductase**, killed rat hepatoma 3924A cells in tissue culture after 7 days of incubation. A concn. of 15 .mu.M caused 50% inhibition of colony-forming ability (IC50). Under the same conditions, hydroxyurea [127-07-1], also an inhibitor of **ribonucleotide reductase**, had an IC50 of 52 .mu.M. Treatment for 1 h with VF 122 of exponentially growing culture resulted in a biphasic exponential dose-response curve. In plateau-phase cells, a threshold exponential curve was obtained. Exponentially growing hepatoma 3924A cells were more sensitive to VF 122 than were plateau-phase cultures. In contrast, hydroxyurea killed only exponentially growing 3924A hepatoma cells, exhibiting an exponential plateau dose-response curve without achieving an IC50 value at concns. from 1 to 200 mM. In synchronized cultures, VF 122 (1 mM for 1 h) was toxic for cells in mid and late G1 phase, in early and mid S phase, and, to a lesser degree, in G2 phase. Hydroxyurea (10 mM for 1 h) killed cells only in S phase. Proliferating and resting hepatoma 3924A cells recovered from sublethal and potentially lethal damage induced by VF 122.
IT **69839-82-3**
RL: PRP (Properties)
(cytotoxicity of, in hepatoma, cell division in relation to)

L68 ANSWER 34 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1982:538288 HCAPLUS

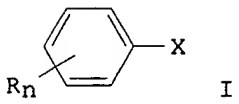
DN 97:138288
TI Modulation of cytarabine metabolism in the human promyelocytic leukemia cell line HL-60 by polyhydroxy-substituted benzohydroxamic acids
AU Howell, Stephen B.; Gill, Susan; **Elford, Howard L.**
CS Cancer Cent., Univ. California, La Jolla, CA, USA
SO Cancer Treat. Rep. (1982), 66(10), 1825-9
CODEN: CTRRDO; ISSN: 0361-5960
DT Journal
LA English
GI



I

AB Two potent new **ribonucleotide reductase** inhibitors, VF 122 (3,4,5-trihydroxybenzohydroxamic acid) [**69839-82-3**] and VF 147 (3,4-dihydroxybenzohydroxamic acid) [**69839-83-4**], were investigated for their ability to modulate the cellular pharmacol. of ara-C (I) [147-94-4] in HL-60 cells. VF 122 and VF 147 increased the total cellular uptake of ara-C by 8% and 29%, resp., when measured 2 h after the start of exposure to 0.1 .mu.M ara-C. This effect was evident after only 10 min of exposure to the **ribonucleotide reductase** inhibitor and did not vary significantly over the concn. range of 10-100 .mu.M for either agent. VF 122 enhanced the incorporation of the ara-C metabolite, ara-CTP [13191-15-6] into DNA by 3.6-fold; VF 147 produced a 5.6-fold increase. In comparison, the max. enhancement achievable with hydroxyurea was 2.1-fold, and with thymidine was 1.8-fold.
IT **69839-82-3 69839-83-4**
RL: BIOL (Biological study)
(ara C metab. and uptake by human leukemia enhancement by, **neoplasm** inhibition in relation to)

L68 ANSWER 35 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1981:543840 HCAPLUS
DN 95:143840
TI Regulation of **ribonucleotide reductase** in mammalian cells by chemotherapeutic agents
AU **Elford, Howard L.**; Van't Riet, Bart; Wampler, Galen L.; Lin, Alan L.; Elford, Roberta M.
CS Cancer Cent., Med. Coll. Virginia, Richmond, VA, 23298, USA
SO Adv. Enzyme Regul. (1981), 19, 151-68
CODEN: AEZRA2; ISSN: 0065-2571
DT Journal
LA English
GI



I

AB Polyhydroxy arom. derivs. I (R = H, OH, Me, OMe; X = COOH, COOMe, COOPh, CONH2, CONHMe, CONHNH2, CONHOH, CH2NH2, etc.; n = 1-3) were tested for **ribonucleotide reductase** [**9040-57-7**]-inhibiting and **antitumor** activity; the most active derivs. had adjacent hydroxy groups. The most effective enzyme inhibitor, 2,3,4-trihydroxybenzohydroxamic acid (I; R = OH, X = CONHOH) [**22372-31-2**] is 145 times more effective than hydroxyurea. However, the best antileukemic compd. is 3,4-dihydroxybenzohydroxamic acid (I; R = OH, X = CONHOH) [**69839-83-4**], which increased the life span of L 1210 leukemic mice >100%. Structure-activity studies revealed that the hydroxamic moiety is not essential for activity. The polyhydroxybenzene derivs. reduced the pool sizes of all 4 deoxynucleotides; hydroxyurea depletes only the deoxypurines. The mechanism of inhibition of the tested compds. appears to be related to their ability to trap free radicals, since there is good correspondence between reductase inhibition and free radical destruction. Dopa analogs were also inhibitory to **ribonucleotide reductase**. The tested compds. also gave elevated reductase levels in the cell. Other cell cycle inhibitors that block from late G1 through early G2 also cause an enhanced level of **ribonucleotide reductase**; however, agents that block in early or mid-G1 or mid or late G2 and mitosis produce lower reductase levels. Thus, reductase synthesis appears to be initiated at the G1/S transition point and this enhanced level of activity continues until late S or G2.

IT **9040-57-7**
RL: PROC (Process)
(inhibition of, by polyhydroxybenzoic acid derivs., **antitumor** activity in relation to)

IT **99-24-1 618-73-5 2150-43-8 2150-44-9 2150-45-0 2150-46-1 2150-47-2 2411-83-8 16053-97-7 22372-31-2 27286-93-7 30697-84-8 35318-15-1 35318-17-3 54337-90-5 56128-66-6 69839-82-3 69839-83-4 70022-11-6 70022-13-8**
RL: BIOL (Biological study)
(**neoplasm** and **ribonucleotide reductase** inhibition by, structure in relation to)

L68 ANSWER 36 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1981:480517 HCAPLUS
DN 95:80517
TI Hydroxy benzohydroxamic acids and benzamides
IN Van't Riet, Bartholomeus; **Elford, Howard L.**; Wampler, Galen L.
PA USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 4263322	A	19810421	US 79-16472	19790301
	US 4394389	A	19830719	US 81-247171	19810324
	US 4448730	A	19840515	US 82-370023	19820420
PRAI	US 79-16472	19790301			
	US 81-247171	19810324			

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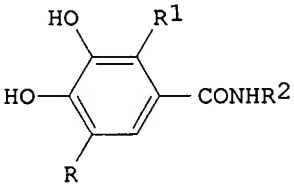


I

AB Title compds. I (R and R1 are H or OH, R2 is H or OH) were prepd. and they inhibited **ribonucleotide reductase**. Thus, 2,3,4-(HO)3C6H2CO2Me was treated with HONH2.1/2H2SO4 and Na2SO3 to give I (R = H, R1 = R2 = OH).

IT **99-24-1 2150-43-8 2150-44-9 2150-46-1 2150-47-2 2411-83-8**
RL: RCT (Reactant)
(amidation of, by hydroxylamine)

IT **618-73-5 54337-90-5 70022-11-6**
RL: RCT (Reactant)
(inhibition of **ribonucleotide reductase** by)

IT **9040-57-7**
RL: RCT (Reactant)
(inhibitors for, hydroxybenzohydroxamic acids and -benzamides as)

IT **2150-45-0P 56128-66-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, by hydroxylamine)

IT **16053-97-7P 22372-31-2P 27286-93-7P 30697-84-8P 35318-15-1P 35318-17-3P 69839-82-3P 69839-83-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, and inhibition of **ribonucleotide reductase** by)

L68 ANSWER 37 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1980:560961 HCAPLUS
DN 93:160961
TI Structure-activity relationships of benzohydroxamic acid inhibitors of **ribonucleotide reductase**
AU Van't Riet, Bart; Kier, Lemont B.; **Elford, Howard L.**
CS Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
SO J. Pharm. Sci. (1980), 69(7), 856-7
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB A structure-activity relationship study of 28 substituted benzohydroxamic acids that inhibit **ribonucleotide reductase** [**9040-57-7**] was undertaken to discern the structural features of the mol. contributing to the inhibitory potency of these compds. An equation contg. 3 mol. connectivity indexes, but not including Hammett

.sigma. values, was developed which gives close correlation with obsd. values for **ribonucleotide reductase** inhibition. It is postulated that the inhibitory potency involves 2 parts of the benzohydroxamic acid mol. One is the hydroxamic portion, which complexes with the metal component of the enzyme, providing a qual. effect. The other is an interaction involving the benzene ring and its substituents and may provide the quant. aspect of the obsd. inhibition values.

IT **9040-57-7**
RL: BIOL (Biological study)
(inhibitors of, benzohydroxamic acids as, structure in relation to)

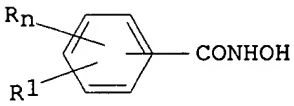
IT **16053-97-7 22372-31-2 27286-93-7 30697-84-8 35318-15-1 35318-17-3 69839-82-3 69839-83-4**
RL: BIOL (Biological study)
(**ribonucleotide reductase** inhibition by, mol. structure in relation to)

L68 ANSWER 38 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1979:179918 HCAPLUS
DN 90:179918
TI New **ribonucleotide reductase** inhibitors with **antineoplastic** activity
AU **Elford, Howard L.**; Wampler, Galen L.; Van't Riet, Bart
CS Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, Va., USA
SO Cancer Res. (1979), 39(3), 844-51
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB For the purpose of developing an effective **anticancer** agent with a mode of action directed against **ribonucleotide reductase** [**9040-57-7**], a no. of acyl and aryl hydroxamic acids and their congeners were tested for their ability to inhibit **ribonucleotide reductase** in vitro and to prolong the life span of L1210 leukemia-bearing mice. Benzohydroxamic acid [495-18-1] and other 6-member arom. ring hydroxamic acids were as inhibitory as was hydroxyurea in vitro, and they increased the life span of L1210 leukemia-bearing mice. Addn. of hydroxy groups to the benzene ring of benzohydroxamic acid increased both inhibition of **ribonucleotide reductase** and life span of L1210 leukemic mice. Di- and trihydroxybenzohydroxamic acids, particularly when the hydroxyl groups were adjacent, were even more potent both in vitro and in vivo. For example, in comparison to hydroxyurea, 2,3,4-trihydroxybenzohydroxamic acid [**22372-31-2**] was 160 times more potent as an inhibitor of **ribonucleotide reductase** and increased the life span of L1210-leukemic mice at a lower dosage. The hydroxamic acid moiety was not essential for activity since 2,3,4-trihydroxybenzamide [**70022-11-6**] was 100 times more potent than was hydroxyurea in vitro. Of the compds. tested, 3,4-dihydroxybenzohydroxamic acid [**69839-83-4**] was most effective in prolonging the life span of L1210-leukemic mice, increasing survival time over 100%, and at one-third the dosage of hydroxyurea.

IT **99-24-1 618-73-5 2150-43-8 2150-44-9 2150-45-0 2150-46-1 2150-47-2 2411-83-8 16053-97-7 22372-31-2 27286-93-7 30697-84-8 35318-15-1 35318-17-3 54337-90-5 56128-66-6 69839-82-3 69839-83-4 70022-11-6 70022-13-8**
RL: BIOL (Biological study)

(**antitumor** activity and **ribonucleotide reductase** inhibition by)
IT **9040-57-7**
RL: BIOL (Biological study)
(inhibitors of, as **neoplasm** inhibitors)

L68 ANSWER 39 OF 39 HCAPLUS COPYRIGHT 1999 ACS
AN 1979:179911 HCAPLUS
DN 90:179911
TI Synthesis of hydroxy- and amino-substituted benzohydroxamic acids: inhibition of **ribonucleotide reductase** and **antitumor** activity
AU Van't Riet, Bart; Wampler, Galen L.; **Elford, Howard L.**
CS Med. Coll. Virginia, Virginia Commonwealth Univ., Richmond, Va., USA
SO J. Med. Chem. (1979), 22(5), 589-92
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I

AB Seventeen title compds. I (R and R1 = H, OH, or NH2; n = 0-3), 5 new and 12 previously reported, were synthesized and tested for **antitumor** activity in L1210 leukemic mice and for mammalian **ribonucleotide reductase** [**9040-57-7**]-inhibitory activity. I(R = 2,3,4-OH, R = H, n=3) [**22372-31-2**] was the most potent enzyme inhibitor (ID50 = 3.5 .mu.M), 140 times more potent than hydroxyurea, but its toxicity limited the **antitumor** activity to a 30% increase in life span (125 mg/kg/day, i.p., for 8 days). The most effective **antitumor** agent was I(R = 3, 4-OH, R1 = H, n = 2) [**69839-83-4**] which prolonged the life span of the L1210 bearing mice.
IT **9040-57-7**
RL: PROC (Process)
(inhibition of, by benzohydroxamides, **antitumor** activity in relation to)
IT **16053-97-7P 22372-31-2P 27286-93-7P 30697-84-8P 35318-15-1P 35318-17-3P 69839-82-3P 69839-83-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **neoplasm**- and **ribonucleotide reductase**-inhibiting activities of)

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DICTIONARY FILE UPDATES: 29 MAR 99 HIGHEST RN 220764-97-6

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L69 33 L54 NOT (L62 OR L19)

remaining hit cmpds from ref 1-33, L68

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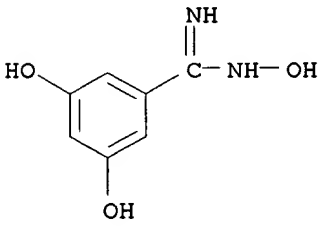
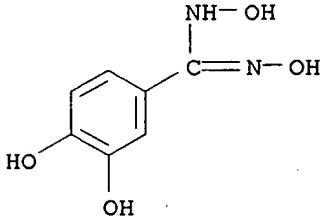
L69 ANSWER 1 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **214692-31-6** REGISTRY
CN Benzenecarboximidamide, N,3,5-trihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN VF 268
FS 3D CONCORD
MF C7 H8 N2 O3
SR CA
LC STN Files: CA, CAPLUS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:310457

L69 ANSWER 2 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **147510-62-1** REGISTRY
CN Benzenecarboximidamide, N,N',3,4-tetrahydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3,4-Dihydroxybenzohydroxamidoxime
FS 3D CONCORD
MF C7 H8 N2 O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



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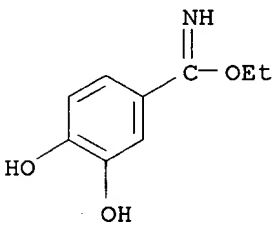
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

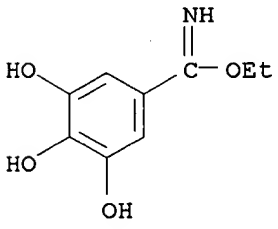
L69 ANSWER 3 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **147510-61-0** REGISTRY
CN Benzenecarboximidic acid, 3,4-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ethyl 3,4-dihydroxybenzimidate
FS 3D CONCORD
MF C9 H11 N O3
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

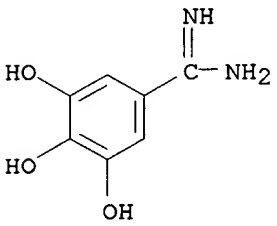
L69 ANSWER 4 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **147510-60-9** REGISTRY
CN Benzenecarboximidic acid, 3,4,5-trihydroxy-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ethyl 3,4,5-trihydroxybenzimidate
FS 3D CONCORD
MF C9 H11 N O4
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

L69 ANSWER 5 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **97186-79-3** REGISTRY
CN Benzenecarboximidamide, 3,4,5-trihydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H8 N2 O3
CI COM
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

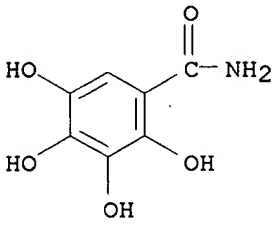


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

REFERENCE 2: 102:166480

L69 ANSWER 6 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **95933-83-8** REGISTRY
CN Benzamide, 2,3,4,5-tetrahydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H7 N O5
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



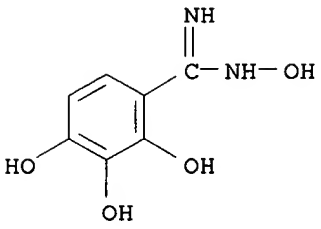
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

REFERENCE 2: 102:166480

L69 ANSWER 7 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **95933-80-5** REGISTRY
CN Benzenecarboximidamide, N,2,3,4-tetrahydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H8 N2 O4

CI COM
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

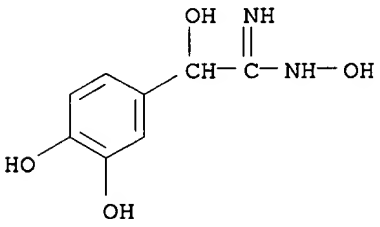


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

REFERENCE 2: 102:166480

L69 ANSWER 8 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **95933-79-2** REGISTRY
CN Benzeneethanimidamide, N,.alpha.,3,4-tetrahydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H10 N2 O4
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

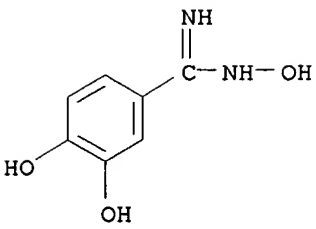


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:20495

REFERENCE 2: 102:166480

L69 ANSWER 9 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **95933-72-5** REGISTRY
CN Benzenecarboximidamide, N,3,4-trihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Amidox
FS 3D CONCORD
DR 125199-74-8
MF C7 H8 N2 O3
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, TOXLINE, TOXLIT, USPATFULL



14 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:177527

REFERENCE 2: 129:310528

REFERENCE 3: 129:310457

REFERENCE 4: 129:156586

REFERENCE 5: 128:149556

REFERENCE 6: 128:31747

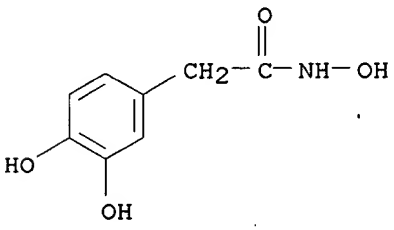
REFERENCE 7: 127:243220

REFERENCE 8: 127:214514

REFERENCE 9: 127:185517

REFERENCE 10: 127:39615

L69 ANSWER 10 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **91362-81-1** REGISTRY
CN Benzeneacetamide, N,3,4-trihydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C8 H9 N O4
LC STN Files: CA, CAPLUS, USPATFULL

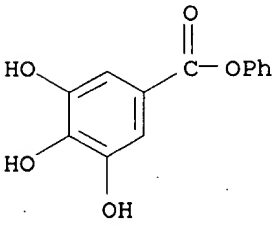


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 101:72459

L69 ANSWER 11 OF 33 REGISTRY COPYRIGHT 1999 ACS

RN **70022-13-8** REGISTRY
CN Benzoic acid, 3,4,5-trihydroxy-, phenyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Phenyl 3,4,5-trihydroxybenzoate
CN Phenyl gallate
FS 3D CONCORD
MF C13 H10 O5
CI COM
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:208318

REFERENCE 2: 107:226075

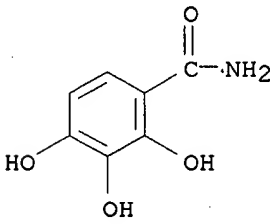
REFERENCE 3: 101:72459

REFERENCE 4: 99:169526

REFERENCE 5: 95:143840

REFERENCE 6: 90:179918

L69 ANSWER 12 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **70022-11-6** REGISTRY
CN Benzamide, 2,3,4-trihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2,3,4-Trihydroxybenzamide
FS 3D CONCORD
MF C7 H7 N O4
LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:230109

REFERENCE 2: 119:20495

REFERENCE 3: 102:166480

REFERENCE 4: 101:72459

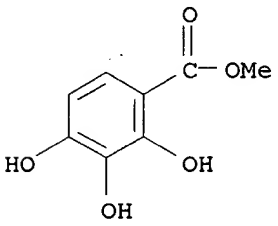
REFERENCE 5: 99:169526

REFERENCE 6: 95:143840

REFERENCE 7: 95:80517

REFERENCE 8: 90:179918

L69 ANSWER 13 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **56128-66-6** REGISTRY
CN Benzoic acid, 2,3,4-trihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Methyl 2,3,4-trihydroxybenzoate
FS 3D CONCORD
MF C8 H8 O5
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, HODOC*, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



17 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:314419

REFERENCE 2: 126:199313

REFERENCE 3: 126:135627

REFERENCE 4: 125:86316

REFERENCE 5: 123:340160

REFERENCE 6: 122:230109

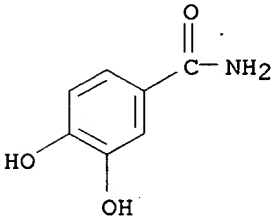
REFERENCE 7: 114:185075

REFERENCE 8: 114:132869

REFERENCE 9: 113:181189

REFERENCE 10: 101:72459

L69 ANSWER 14 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **54337-90-5** REGISTRY
CN Benzamide, 3,4-dihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3,4-Dihydroxybenzamide
CN 4-Carbamoyl-1,2-benzenediol
FS 3D CONCORD
MF C7 H7 N O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:230109

REFERENCE 2: 106:46991

REFERENCE 3: 103:83953

REFERENCE 4: 101:72459

REFERENCE 5: 99:169526

REFERENCE 6: 95:143840

REFERENCE 7: 95:80517

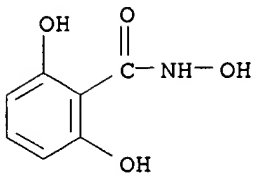
REFERENCE 8: 93:89445

REFERENCE 9: 90:179918

REFERENCE 10: 85:116459

L69 ANSWER 15 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **35318-17-3** REGISTRY
CN Benzamide, N,2,6-trihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .gamma.-Resorcylohydroxamic acid (8CI)
OTHER NAMES:
CN 2,6-Dihydroxybenzohydroxamic acid
CN 2,6-Dihydroxybenzoylhydroxamic acid
CN 2,6-Dihydroxyphenylhydroxamic acid
DR 16110-22-8
MF C7 H7 N O4

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



12 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:265724

REFERENCE 2: 128:176932

REFERENCE 3: 122:230109

REFERENCE 4: 120:26122

REFERENCE 5: 101:72459

REFERENCE 6: 99:169526

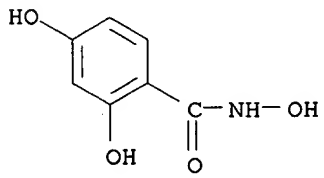
REFERENCE 7: 95:143840

REFERENCE 8: 95:80517

REFERENCE 9: 93:160961

REFERENCE 10: 90:179918

L69 ANSWER 16 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **35318-15-1** REGISTRY
CN Benzamide, N,2,4-trihydroxy- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2,4-Dihydroxybenzohydroxamic acid
CN 2,4-Dihydroxybenzoylhydroxamic acid
CN 2,4-Dihydroxyphenylhydroxamic acid
FS 3D CONCORD
MF C7 H7 N O4
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:230109

REFERENCE 2: 121:270375

REFERENCE 3: 120:123329

REFERENCE 4: 120:26122

REFERENCE 5: 101:72459

REFERENCE 6: 99:169526

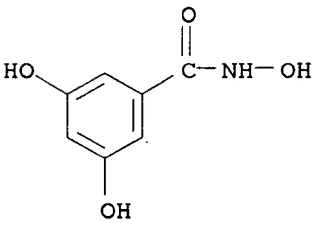
REFERENCE 7: 95:143840

REFERENCE 8: 95:80517

REFERENCE 9: 93:160961

REFERENCE 10: 90:179918

L69 ANSWER 17 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **30697-84-8** REGISTRY
CN Benzamide, N,3,5-trihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .alpha.-Resorcylohydroxamic acid (8CI)
OTHER NAMES:
CN 3,5-Dihydroxybenzohydroxamic acid
CN 3,5-Dihydroxyphenylhydroxamic acid
CN 3,5-Resorcylohydroxamic acid
FS 3D CONCORD
MF C7 H7 N O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:230109

REFERENCE 2: 120:26122

REFERENCE 3: 101:72459

REFERENCE 4: 99:169526

REFERENCE 5: 95:143840

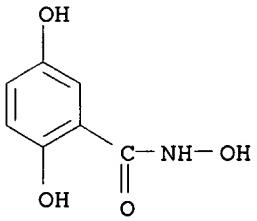
REFERENCE 6: 95:80517

REFERENCE 7: 93:160961

REFERENCE 8: 90:179918

REFERENCE 9: 90:179911

L69 ANSWER 18 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **27286-93-7** REGISTRY
CN Benzamide, N,2,5-trihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gentisohydroxamic acid (8CI)
OTHER NAMES:
CN 2,5-Dihydroxybenzohydroxamic acid
CN 2,5-Dihydroxyphenylhydroxamic acid
FS 3D CONCORD
MF C7 H7 N O4
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, MEDLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



18 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:265724

REFERENCE 2: 122:230109

REFERENCE 3: 121:270375

REFERENCE 4: 120:26122

REFERENCE 5: 117:233527

REFERENCE 6: 106:478

REFERENCE 7: 105:75714

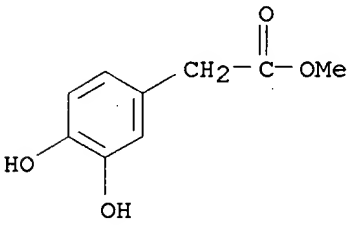
REFERENCE 8: 101:72459

REFERENCE 9: 99:169526

REFERENCE 10: 99:2939

L69 ANSWER 19 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **25379-88-8** REGISTRY
CN Benzeneacetic acid, 3,4-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:
CN Acetic acid, (3,4-dihydroxyphenyl)-, methyl ester (8CI)
OTHER NAMES:
CN Methyl 3,4-dihydroxyphenylacetate
FS 3D CONCORD
MF C9 H10 O4
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



20 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
20 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:350180

REFERENCE 2: 126:314871

REFERENCE 3: 124:146174

REFERENCE 4: 124:37685

REFERENCE 5: 123:227576

REFERENCE 6: 123:167983

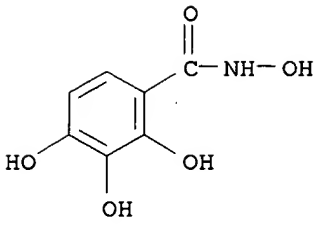
REFERENCE 7: 122:160689

REFERENCE 8: 117:49056

REFERENCE 9: 114:6546

REFERENCE 10: 112:138764

L69 ANSWER 20 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **22372-31-2** REGISTRY
CN Benzamide, N,2,3,4-tetrahydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzohydroxamic acid, 2,3,4-trihydroxy- (8CI)
OTHER NAMES:
CN 2,3,4-Trihydroxybenzohydroxamic acid
CN 2,3,4-Trihydroxybenzoylhydroxamic acid
CN 2,3,4-Trihydroxyphenylhydroxamic acid
FS 3D CONCORD
DR 106573-40-4
MF C7 H7 N O5
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



14 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:230109

REFERENCE 2: 120:26122

REFERENCE 3: 109:162929

REFERENCE 4: 106:60880

REFERENCE 5: 101:72459

REFERENCE 6: 99:169526

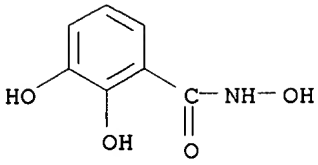
REFERENCE 7: 99:47639

REFERENCE 8: 98:49384

REFERENCE 9: 95:143840

REFERENCE 10: 95:80517

L69 ANSWER 21 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **16053-97-7** REGISTRY
CN Benzamide, N,2,3-trihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN o-Pyrocatechuohydroxamic acid (8CI)
OTHER NAMES:
CN 2,3-Dihydroxybenzohydroxamic acid
CN 2,3-Dihydroxybenzohydroximic acid
CN 2,3-Dihydroxybenzoylhydroxamic acid
CN 2,3-Dihydroxyphenylhydroxamic acid
FS 3D CONCORD
DR 16063-90-4
MF C7 H7 N O4
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



17 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:310457

REFERENCE 2: 128:265724

REFERENCE 3: 122:230109

REFERENCE 4: 120:26122

REFERENCE 5: 105:75714

REFERENCE 6: 101:72459

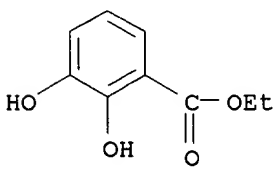
REFERENCE 7: 99:169526

REFERENCE 8: 99:2939

REFERENCE 9: 96:45862

REFERENCE 10: 95:143840

L69 ANSWER 22 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **3943-73-5** REGISTRY
CN Benzoic acid, 2,3-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN o-Pyrocatechuic acid, ethyl ester (7CI, 8CI)
OTHER NAMES:
CN Ethyl 2,3-dihydroxybenzoate
CN Pyrocatechuic acid ethyl ester
FS 3D CONCORD
MF C9 H10 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



12 REFERENCES IN FILE CA (1967 TO DATE)
12 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 125:275801

REFERENCE 2: 123:188481

REFERENCE 3: 122:132767

REFERENCE 4: 119:139245

REFERENCE 5: 109:92747

REFERENCE 6: 108:68326

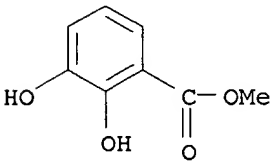
REFERENCE 7: 86:89431

REFERENCE 8: 84:89845

REFERENCE 9: 82:124999

REFERENCE 10: 80:14747

L69 ANSWER 23 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2411-83-8** REGISTRY
CN Benzoic acid, 2,3-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN o-Pyrocatechuic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2,3-Dihydroxybenzoic acid methyl ester
CN Methyl 2,3-dihydroxybenzoate
FS 3D CONCORD
MF C8 H8 O4
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



71 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
71 REFERENCES IN FILE CAPLUS (1967 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 129:108271

REFERENCE 2: 128:257432

REFERENCE 3: 128:228056

REFERENCE 4: 128:153984

REFERENCE 5: 128:61358

REFERENCE 6: 127:173149

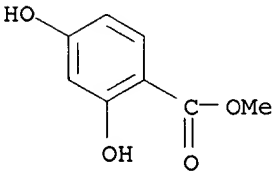
REFERENCE 7: 127:149263

REFERENCE 8: 127:26111

REFERENCE 9: 126:117791

REFERENCE 10: 125:297034

L69 ANSWER 24 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2150-47-2** REGISTRY
CN Benzoic acid, 2,4-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .beta.-Resorcylic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2,4-Dihydroxybenzoic acid methyl ester
CN Methyl .beta.-resorcylate
CN Methyl 2,4-dihydroxybenzoate
FS 3D CONCORD
MF C8 H8 O4
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, HODOC*, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



168 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
168 REFERENCES IN FILE CAPLUS (1967 TO DATE)
11 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:182359

REFERENCE 2: 130:119075

REFERENCE 3: 130:92789

REFERENCE 4: 129:330553

REFERENCE 5: 129:325737

REFERENCE 6: 129:276050

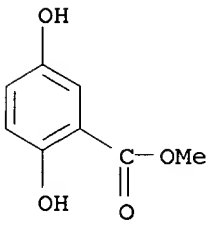
REFERENCE 7: 129:259609

REFERENCE 8: 129:230908

REFERENCE 9: 129:161815

REFERENCE 10: 129:156467

L69 ANSWER 25 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2150-46-1** REGISTRY
CN Benzoic acid, 2,5-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gentisic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2,5-Dihydroxybenzoic acid methyl ester
CN Methoxycarbonylhydroquinone
CN Methyl 2,5-dihydroxybenzoate
CN Methyl gentisate
FS 3D CONCORD
MF C8 H8 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



129 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
129 REFERENCES IN FILE CAPLUS (1967 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 129:330553

REFERENCE 2: 129:301914

REFERENCE 3: 129:276050

REFERENCE 4: 129:230266

REFERENCE 5: 129:175374

REFERENCE 6: 129:108921

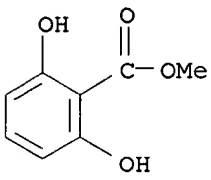
REFERENCE 7: 129:108271

REFERENCE 8: 128:192414

REFERENCE 9: 128:75560

REFERENCE 10: 127:346543

L69 ANSWER 26 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2150-45-0** REGISTRY
CN Benzoic acid, 2,6-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .gamma.-Resorcylic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN Methyl 2,6-dihydroxybenzoate
FS 3D CONCORD
MF C8 H8 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CSCHEM, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



59 REFERENCES IN FILE CA (1967 TO DATE)
60 REFERENCES IN FILE CAPLUS (1967 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:153665

REFERENCE 2: 130:138573

REFERENCE 3: 129:37503

REFERENCE 4: 128:180230

REFERENCE 5: 128:88670

REFERENCE 6: 127:148996

REFERENCE 7: 126:144254

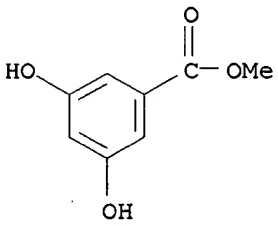
REFERENCE 8: 126:117791

REFERENCE 9: 126:74592

REFERENCE 10: 125:86314

L69 ANSWER 27 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2150-44-9** REGISTRY
CN Benzoic acid, 3,5-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN .alpha.-Resorcylic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN .alpha.-Resorcinol carboxylic acid methyl ester
CN 3,5-Dihydroxybenzoic acid methyl ester

CN Methyl .alpha.-resorcylate
CN Methyl 3,5-dihydroxybenzoate
FS 3D CONCORD
MF C8 H8 O4
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, HODOC*, IFICDB, IFIPAT, IFIUDB, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



191 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
193 REFERENCES IN FILE CAPLUS (1967 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:182854

REFERENCE 2: 130:153665

REFERENCE 3: 130:139723

REFERENCE 4: 130:121859

REFERENCE 5: 130:81345

REFERENCE 6: 130:73852

REFERENCE 7: 130:52210

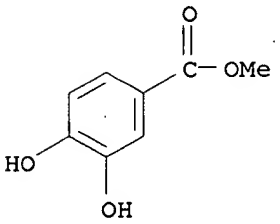
REFERENCE 8: 130:1593

REFERENCE 9: 129:330553

REFERENCE 10: 129:283338

L69 ANSWER 28 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **2150-43-8** REGISTRY
CN Benzoic acid, 3,4-dihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Protocatechuic acid, methyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN 3,4-Dihydroxybenzoic acid methyl ester
CN Methyl 3,4-dihydroxybenzoate
CN Methyl protocatechuate
FS 3D CONCORD
DR 118074-32-1
MF C8 H8 O4

CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CSCHEM, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, NAPRALERT, SPECINFO, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



134 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
134 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:182439

REFERENCE 2: 130:90083

REFERENCE 3: 130:59147

REFERENCE 4: 129:276058

REFERENCE 5: 129:260405

REFERENCE 6: 129:230850

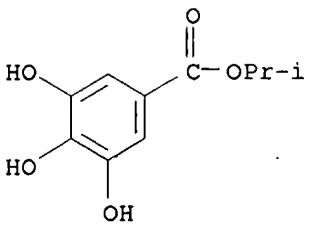
REFERENCE 7: 129:216964

REFERENCE 8: 129:11964

REFERENCE 9: 128:257428

REFERENCE 10: 128:203020

L69 ANSWER 29 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **1138-60-9** REGISTRY
CN Benzoic acid, 3,4,5-trihydroxy-, 1-methylethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gallic acid, isopropyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN Isopropyl gallate
FS 3D CONCORD
MF C10 H12 O5
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, HODOC*, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



33 REFERENCES IN FILE CA (1967 TO DATE)
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:168066

REFERENCE 2: 130:139145

REFERENCE 3: 129:345287

REFERENCE 4: 129:316016

REFERENCE 5: 129:230498

REFERENCE 6: 127:298548

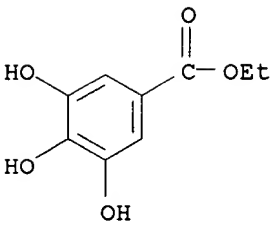
REFERENCE 7: 126:288106

REFERENCE 8: 126:54866

REFERENCE 9: 124:277987

REFERENCE 10: 123:231180

L69 ANSWER 30 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **831-61-8** REGISTRY
CN Benzoic acid, 3,4,5-trihydroxy-, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gallic acid, ethyl ester (6CI, 8CI)
CN Phyllemblin (7CI)
OTHER NAMES:
CN 3,4,5-Trihydroxybenzoic acid ethyl ester
CN Ethyl 3,4,5-trihydroxybenzoate
CN Ethyl gallate
CN Nipa No. 48
CN Nipagallin A
CN Progallin A
FS 3D CONCORD
DR 52441-13-1
MF C9 H10 O5
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NAPRALERT, NIOSHTIC, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



306 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
307 REFERENCES IN FILE CAPLUS (1967 TO DATE)
38 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:147718

REFERENCE 2: 130:139145

REFERENCE 3: 130:122185

REFERENCE 4: 130:67782

REFERENCE 5: 130:66148

REFERENCE 6: 129:345287

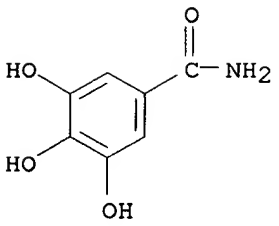
REFERENCE 7: 129:330553

REFERENCE 8: 129:316016

REFERENCE 9: 129:301849

REFERENCE 10: 129:276050

L69 ANSWER 31 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **618-73-5** REGISTRY
CN Benzamide, 3,4,5-trihydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gallamide (6CI, 7CI, 8CI)
OTHER NAMES:
CN 3,4,5-Trihydroxybenzamide
CN 3,4,5-Trihydroxybenzoic acid amide
CN Gallic acid amide
FS 3D CONCORD
MF C7 H7 N O4
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, HODOC*, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



21 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
21 REFERENCES IN FILE CAPLUS (1967 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:99961

REFERENCE 2: 129:137546

REFERENCE 3: 126:220714

REFERENCE 4: 125:33284

REFERENCE 5: 124:254237

REFERENCE 6: 124:7312

REFERENCE 7: 122:230109

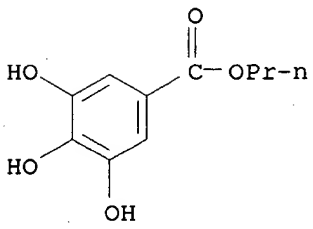
REFERENCE 8: 116:257014

REFERENCE 9: 113:98988

REFERENCE 10: 106:76353

L69 ANSWER 32 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **121-79-9** REGISTRY
CN Benzoic acid, 3,4,5-trihydroxy-, propyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gallic acid, propyl ester (6CI, 8CI)
OTHER NAMES:
CN n-Propyl 3,4,5-trihydroxybenzoate
CN n-Propyl gallate
CN Nipa 49
CN Nipagallin P
CN Nipanox S 1
CN PG
CN Progallin P
CN Propyl 3,4,5-trihydroxybenzoate
CN Propyl gallate
CN Tenox PG
FS 3D CONCORD
DR 56274-95-4
MF C10 H12 O5
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB,

IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



1717 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1717 REFERENCES IN FILE CAPLUS (1967 TO DATE)
150 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:187051

REFERENCE 2: 130:181693

REFERENCE 3: 130:179408

REFERENCE 4: 130:167414

REFERENCE 5: 130:165371

REFERENCE 6: 130:165131

REFERENCE 7: 130:158466

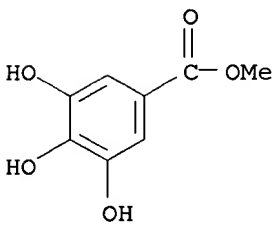
REFERENCE 8: 130:158283

REFERENCE 9: 130:149655

REFERENCE 10: 130:147718

L69 ANSWER 33 OF 33 REGISTRY COPYRIGHT 1999 ACS
RN **99-24-1** REGISTRY
CN Benzoic acid, 3,4,5-trihydroxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Gallic acid, methyl ester (6CI, 8CI)
OTHER NAMES:
CN 3,4,5-Trihydroxybenzoic acid methyl ester
CN Methyl 3,4,5-trihydroxybenzoate
CN Methyl gallate
FS 3D CONCORD
MF C8 H8 O5
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,

MRCK*, NAPRALERT, NIOSHTIC, PIRA, RTECS*, SPECINFO, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



488 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
488 REFERENCES IN FILE CAPLUS (1967 TO DATE)
34 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 130:165371

REFERENCE 2: 130:131783

REFERENCE 3: 130:121146

REFERENCE 4: 130:66148

REFERENCE 5: 130:24895

REFERENCE 6: 130:24852

REFERENCE 7: 130:18938

REFERENCE 8: 130:10501

REFERENCE 9: 130:8937

REFERENCE 10: 130:4241

=> d his l70-

(FILE 'HCAPLUS' ENTERED AT 14:52:22 ON 30 MAR 1999)
L70 82 S L21 AND ?INFLAM?
L71 85 S L21 AND ?INFECT?
L72 40 S L21 AND ?STRESS?
L73 5 S L70-L72 AND L24
L74 1 S L73 NOT L68
L75 187 S PROTEIN KINASE B
S 191808-15-8/REG#

FILE 'REGISTRY' ENTERED AT 14:54:15 ON 30 MAR 1999
L76 1 S 191808-15-8/RN

FILE 'HCAPLUS' ENTERED AT 14:54:15 ON 30 MAR 1999
L77 23 S L76
L78 1 S L21 AND L75,L77

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L79           0 S L78 NOT L68
L80          26 S L21 AND CHEMOTHERAP?
L81         991 S L21 AND (OXIDANT OR ANTIOXIDANT OR OXIDIZING AGENT)

=> d his l83-

     (FILE 'HCAPLUS' ENTERED AT 14:54:15 ON 30 MAR 1999)
L83           5 S L82 NOT L68

     FILE 'USPATFULL' ENTERED AT 14:57:01 ON 30 MAR 1999
L84           8 S L62

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 14:57:11 ON 30 MAR 1999
L85          12 DUP REM L83 L84 (1 DUPLICATE REMOVED)

=> d bib abs hitrn tot

L85  ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 1999 ACS       DUPLICATE 1
AN   1995:278447  HCAPLUS
DN   122:96513
TI   Method of treating hemoglobinopathies with polyhydroxy benzoic, mandelic
     or phenylacetic acid deriv. to increase fetal Hb
IN   Elford, Howard L.; Van T. Riet, Bartholomeus
PA   USA
SO   U.S., 5 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   US 5366996          A    19941122       US 92-986861     19921207
OS   MARPAT 122:96513
AB   A therapeutic process for treating anemias in primates, including man,
     particularly those anemias of genetic origin including sickle-cell anemia,
     comprises administering to an anemic primate an amt. of a polyhydroxy
     benzoic, mandelic or phenylacetic in acid deriv. as specified at a dose
     level sufficient to increase fetal Hb.  In an anemic baboon model,
     induction of fetal cells and fetal reticulocytes by 3,4-
     dihydroxybenzohydroxamic acid were equal or superior to other
     cytoreductive agents with less myelosuppression.
IT   69839-83-4, 3,4-Dihydroxybenzohydroxamic acid
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (hemoglobinopathy treatment with polyhydroxy benzoic, mandelic or
        phenylacetic acid deriv. to increase fetal Hb)

L85  ANSWER 2 OF 12  HCAPLUS  COPYRIGHT 1999 ACS
AN   1994:236198  HCAPLUS
DN   120:236198
TI   Therapeutic process for the treatment of septic shock using
     polyhydroxy-substituted benzamide or phenylacetamide derivative
IN   Elford, Howard L.; Van T. Riet, Bartholomeus
PA   USA
SO   PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
```

) other patents for L62

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9402135	A1	19940203	WO 93-US6990	19930726
	W: JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5350770	A	19940927	US 92-919907	19920728
PRAI	US 92-919907	19920728			

AB Septic shock is prevented and/or treated by administration of a polyhydroxy-substituted benzamide or phenylacetamide deriv. to a human suffering from, or in danger of contracting, septic shock. Didox prolonged the life of mice with LPS-induced septic shock.

IT **69839-83-4**, Didox
RL: BIOL (Biological study)
(septic shock and septicemia treatment with)

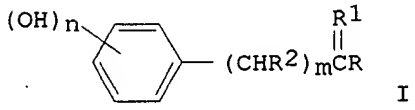
L85 ANSWER 3 OF 12 USPATFULL
AN 94:84277 USPATFULL
TI Therapeutic process for the treatment of septic shock
IN Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
PI US 5350770 19940927
AI US 92-919907 19920728 (7)
DT Utility
EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: Jarvis, William R. A.
LREP Rowe, James L.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 327
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A therapeutic process for treating septic shock comprising the administration of a polyhydroxy-substituted benzamide or phenylacetamide derivative to a human suffering from, or in danger of contracting, septic shock.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **69839-83-4**, Didox
(septic shock and septicemia treatment with)

L85 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:552070 HCAPLUS
DN 119:152070
TI Treating viral diseases with a polyhydroxy benzoic, mandelic or phenylacetic acid derivative
IN Elford, Howard L.; Van T. Riet, Bartholomeus
PA USA
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9312782	A1	19930708	WO 92-US9377	19921029
	W: JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF,				

BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG
EP 610444 A1 19940817 EP 93-904475 19921029
R: CH, DE, ES, FR, GB, IT, LI, SE
PRAI US 91-785982 19911031
WO 92-US9377 19921029
OS MARPAT 119:152070
GI



I

AB The title compd. I (R = NOH, NH2, alkyl OPh; R1 = O, NH, NOH; R2 = H, OH; n = 2-5; m = 0, 1) are drugs for the treatment of diseases caused by DNA viruses or retroviruses. N,3,4-trihydroxybenzamide (450 mg/kg) suppressed in mice splenomegaly caused by Friend leukemia virus infection.
IT **69839-83-4**, N,3,4-Trihydroxybenzamide **95933-74-7**, N,3,4,5-Tetrahydroxybenzimidamide
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(virucide, for treatment of DNA virus and retrovirus infections)

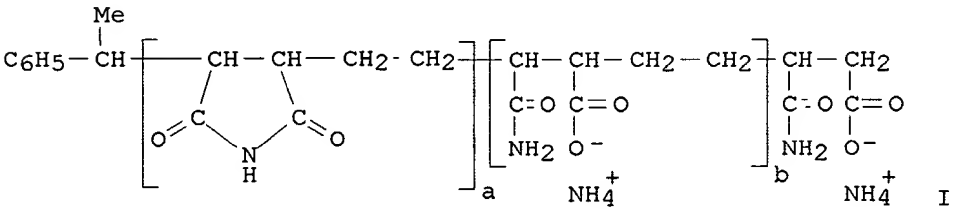
L85 ANSWER 5 OF 12 USPATFULL
AN 93:8844 USPATFULL
TI Polyhydroxybenzoic acid derivatives
IN van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111
PI US 5183828 19930202
AI US 90-555834 19900720 (7)
RLI Continuation-in-part of Ser. No. US 89-302946, filed on 30 Jan 1989, now abandoned which is a division of Ser. No. US 86-907562, filed on 15 Sep 1986, now patented, Pat. No. US 4942253, issued on 17 Jul 1990 which is a division of Ser. No. US 83-497370, filed on 23 May 1983, now patented, Pat. No. US 4623659, issued on 18 Nov 1986
DT Utility
EXNAM Primary Examiner: Waddell, Frederick E.; Assistant Examiner: Criares, T. J.
LREP Rowe, James L.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1040
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **95933-74-7P**
(prepn. of, as ribonucleotide reductase inhibitor and free radical scavenger)

L85 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:99301 HCAPLUS
DN 116:99301
TI Maleic anhydride copolymers as antidotes for the cytotoxicity of neoplasm inhibitors
IN Bach, Ardalan; Shanahan, William R., Jr.
PA Searle, G. D., and Co., USA
SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 393575	A1	19901024	EP 90-107246	19900417
	EP 393575	B1	19940316		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014732	AA	19901017	CA 90-2014732	19900417
	JP 02292227	A2	19901203	JP 90-101530	19900417
	AT 102838	E	19940415	AT 90-107246	19900417
	ES 2062155	T3	19941216	ES 90-107246	19900417
PRAI	US 89-339503	19890417			
	EP 90-107246	19900417			

OS MARPAT 116:99301
GI



I

AB Half-amide:half-imide copolymers comprising ethylene and maleic anhydride moieties (structure given), specifically carbetimer (I; a/b = 1:2-5), decrease the cytotoxic side effects of neoplasm inhibitors. Mice treated i.v. with 21 mg adriamycin/kg died within 5 days. When 1700 mg I/kg was administered concomitantly, no lethality was shown for >30 days.
IT **69839-83-4**, Didox
RL: PRP (Properties)
(cytotoxicity of, maleic anhydride copolymer antidote for)

L85 ANSWER 7 OF 12 USPATFULL
AN 90:56316 USPATFULL
TI Polyhydroxybenzoic acid derivatives
IN van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
Elford, Howard L., 3343 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111

PI US 4942253 19900717
AI US 86-907562 19860915 (6)
RLI Division of Ser. No. US 83-497370, filed on 23 May 1983, now patented, Pat. No. US 4623659
DT Utility
EXNAM Primary Examiner: Sutto, Anton H.
LREP Rowe, James L.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 710
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **95933-74-7P**
(prepn. and antitumor activity of)

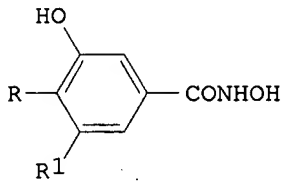
L85 ANSWER 8 OF 12 USPATFULL
AN 86:64952 USPATFULL
TI Polyhydroxybenzoic acid derivatives
IN van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111
PI US 4623659 19861118
AI US 83-497370 19830523 (6)
DT Utility
EXNAM Primary Examiner: Trousof, Natalie; Assistant Examiner: Hendriksen, L.
LREP Ashbrook, Charles W.; Rowe, James L.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1,14
DRWN No Drawings
LN.CNT 742
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polyhydroxy-substituted benz, phenylacet and mandelamidines, amidates, amidoximes and hydroxyamidoximes--ribonucleotide reductase inhibitors, and free radical scavengers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **95933-74-7P**
(prepn. and antitumor activity of)

L85 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 1999 ACS
AN 1985:84438 HCAPLUS
DN 102:84438
TI Oncolytic drug combinations of a hydroxybenzohydroxamic acid and doxorubicin or cyclophosphamide
IN Elford, Howard L.; Wampler, Galen L.; Van't Riet, Bartholomeus
PA USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8404246	A1	19841108	WO 84-US608	19840420
	W: JP				
	RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
	EP 140958	A1	19850515	EP 84-901890	19840420
	EP 140958	B1	19891220		
	R: AT, BE, CH, DE, FR, GB, LI, NL, SE				
	AT 48757	E	19900115	AT 84-901890	19840420
PRAI	US 83-487368	19830421			
	EP 84-901890	19840420			
	WO 84-US608	19840420			

GI



I

AB A synergistic antineoplastic compn. comprises doxorubicin [23214-92-8] or cyclophosphamide [50-18-0] and a hydroxybenzohydroxamic acid I (R and R1 = H or OH). Thus, doxorubicin-HCl [25316-40-9] and 3,4-dihydroxybenzohydroxamic acid (I; R = OH, R1 = H) **[69839-83-4]** administered to mice bearing transplanted L-1210 leukemia at 6 and 275 mg/kg, resp., gave substantial increases in life span plus survivors compared with either compd. by itself.

IT **69839-83-4**
RL: BIOL (Biological study)
(neoplasm inhibiting synergistic compn. contg. doxorubicin or cyclophosphamide and)

L85 ANSWER 10 OF 12 USPATFULL
AN 84:27242 USPATFULL
TI Hydroxybenzohydroxamic acids, benzamides and esters and related compounds as ribonucleotide reductase inhibitors
IN van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111
PI US 4448730 19840515
AI US 82-370023 19820420 (6)
RLI Continuation-in-part of Ser. No. US 81-247171, filed on 24 Mar 1981, now patented, Pat. No. US 4394389 which is a continuation-in-part of Ser. No. US 79-16472, filed on 1 Mar 1979, now patented, Pat. No. US 4263322, issued on 21 Apr 1981
DT Utility
EXNAM Primary Examiner: Killos, Paul J.
LREP Rowe, James L.; Whale, Arthur R.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 575
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Di, tri and tetrahydroxybenzohydroxamic acids, amides and the corresponding di, tri and tetrahydroxy substituted phenylalkanohydroxamic acids, amides and phenyl esters, ribonucleotide reductase inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **69839-82-3P 69839-83-4P**
(prepn. of)

L85 ANSWER 11 OF 12 USPATFULL
AN 83:30480 USPATFULL
TI Hydroxybenzohydroxamic acids, benzamides and esters as ribonucleotide reductase inhibitors
IN van't Riet, Bartholomeus, 3419 Nobel Ave., Richmond, VA, United States 23222
Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111
PI US 4394389 19830719
AI US 81-247171 19810324 (6)
RLI Continuation-in-part of Ser. No. US 79-16472, filed on 1 Mar 1979, now patented, Pat. No. US 4263322, issued on 21 Apr 1981
DT Utility
EXNAM Primary Examiner: Waltz, Thomas A.
LREP Rowe, James L.; Whale, Arthur R.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1,6,8
DRWN No Drawings
LN.CNT 513
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Di and trihydroxybenzohydroxamic acids, amides, alkyl substituted amides and phenyl esters, ribonucleotide reductase inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **69839-82-3P 69839-83-4P**
(prepn. and ribonucleotide reductase-inhibiting and neoplasm-inhibiting activity of)

L85 ANSWER 12 OF 12 USPATFULL
AN 81:21991 USPATFULL
TI Hydroxy benzohydroxamic acids and benzamides
IN van't Riet, Bartholomeus, 3419 Noble Ave., Richmond, VA, United States 23222
Elford, Howard L., 3313 Gloucester Rd., Richmond, VA, United States 23227
Wampler, Galen L., 6938 Chamberlayne Rd., Mechanicsville, VA, United States 23111
PI US 4263322 19810421
AI US 79-16472 19790301 (6)
DT Utility
EXNAM Primary Examiner: Waltz, Thomas A.
LREP Rowe, James L.; Whale, Arthur R.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 235

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Di or trihydroxybenzohydroxamic acids or N-substituted benzamides, inhibitors or ribonucleotide reductase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **69839-82-3P 69839-83-4P**
(prepn. of, and inhibition of ribonucleotide reductase by)

=> fil biosis
FILE 'BIOSIS' ENTERED AT 15:03:31 ON 30 MAR 1999
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 March 1999 (19990317/ED)

The BIOSIS file has been reloaded. Enter HELP RLOAD and HELP REINDEXING for details.

=> d his l86-

(FILE 'BIOSIS' ENTERED AT 14:57:40 ON 30 MAR 1999)

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L86          63 S L62
L87          63 S DIDOX OR TRIMIDOX OR VF122 OR VF147 OR VF()(122 OR 147) OR NS
L88          70 S L86,L87
L89          39 S L88 AND (00520/CC OR (MEETING OR POSTER OR ABSTRACT)(L)IT OR
L90        5996 S L31
L91           1 S L88 AND L90
L92           0 S L89 AND L91
L93        2060 S L19 OR RIBONUCLEOTIDE REDUCTASE
L94          48 S L88 AND L93
L95          25 S L94 AND L89
               E ELFORD H/AU
L96          79 S E3-E6
L97          48 S L96 AND L88
L98          33 S L89 AND L97
L99          25 S L95 AND L98
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FILE 'BIOSIS' ENTERED AT 15:03:31 ON 30 MAR 1999

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L99 ANSWER 1 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:377165 BIOSIS
DN PREV199800377165
TI Novel **ribonucleotide reductase** (RR) inhibitors, **didox** and **trimidox**, produce antiretroviral effects in the murine immunodeficiency (MAIDS) and in the HIV-infected HuPBMC SCID models.
AU **Elford, H. (1)**; Van't Riet, B. (1); Mayhew, C.; Oakley, O.; Piper, J.; Gallicchio, V.; Black, P.; Kunder, S.; Goldberg, G.; Broud, D.; Hall, B.; Bacho, M.; Papermaster, S.; Ussery, M.
CS (1) Molecules For Health Inc., Richmond, VA USA
SO Antiviral Research, (March, 1998) Vol. 37, No. 3, pp. A58.
Meeting Info.: Eleventh International Conference on Antiviral Research San Diego, California, USA April 5-10, 1998 International Society for Antiviral Research

. ISSN: 0166-3542.
DT **Conference**
LA English
CC Chemotherapy - Antiviral Agents *38506
Enzymes - Chemical and Physical *10806
Medical and Clinical Microbiology - Virology *36006
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Retroviridae 02623
Muridae 86375
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection; Pharmacology
IT Diseases
human immunodeficiency virus infection [HIV infection]: viral disease; murine acquired immunodeficiency syndrome: viral disease
IT Chemicals & Biochemicals
didanosine: antiviral - drug, enzyme inhibitor - drug; **didox**: antiviral - drug, enzyme inhibitor - drug; **ribonucleotide reductase**: inhibition; **trimidox**: antiviral - drug, enzyme inhibitor - drug; viral RNA
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Animal Viruses, Viruses, Microorganisms
ORGN Organism Name
human immunodeficiency virus [HIV] (Retroviridae): pathogen; mouse (Muridae): animal model, host
ORGN Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
69839-83-4 (DIDOX)
95933-74-7 (TRIMIDOX)
69655-05-6 (DIDANOSINE)

L99 ANSWER 2 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:197986 BIOSIS
DN PREV199800197986
TI Inhibition of lymphoproliferative and late-stage lymphoma in LP-BM5 murine leukemia virus (MuLV) infection by **ribonucleotide reductase** inhibitors **trimidox** and **didox** alone and in combination with 2',3'-dideoxyinosine (ddI.
AU Mayhew, C. N. (1); Oakley, O. R. (1); Mampuru, L. J.; Hughes, N. K.; **Elford, H. L.**; Greenberg, R.; Phillips, J. D. (1); Birch, N. J. (1); Becker, R. W.; Gallicchio, V. S.
CS (1) Univ. Wolverhampton, Wolverhampton UK
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1998) Vol. 39, pp. 605.
Meeting Info.: 89th Annual Meeting of the American Association for Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998 American Association for Cancer Research
. ISSN: 0197-016X.
DT **Conference**
LA English
CC Pharmacology - Blood and Hematopoietic Agents *22008

Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Chemotherapy - Antiviral Agents *38506
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Retroviridae 02623
Muridae 86375
IT Major Concepts
Infection; Pharmacology; Tumor Biology
IT Diseases
LP-BM5 murine leukemia virus infection: viral disease
IT Chemicals & Biochemicals
didox: antineoplastic - drug, enzyme inhibitor - drug, antiviral - drug, **ribonucleotide reductase** inhibitor; **trimidox**: antineoplastic - drug, antiviral - drug, **ribonucleotide reductase** inhibitor, enzyme inhibitor - drug; 2',3'-dideoxyinosine [ddI]: antiviral - drug
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Animal Viruses, Viruses, Microorganisms
ORGN Organism Name
mouse (Muridae); LP-BM5 murine leukemia virus (Retroviridae)
ORGN Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
95933-74-7 (TRIMIDOX)
69839-83-4 (DIDOX)
69655-05-6 (2',3'-DIDEOXYINOSINE)

L99 ANSWER 3 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:327268 BIOSIS
DN PREV199799626471
TI Inhibition of lymphoma using **ribonucleotide reductase** inhibitors **Didox** or **Trimidox** in the murine immunodeficiency maids model: Alone or in combination with ddI.
AU Gallicchio, Vincent S. (1); Mayhew, C. (1); Oliver, O. (1); Hughes, N. K. (1); Piper, J. (1); **Elford, H. L.**
CS (1) Lucille P. Markey Cancer Cent., Univ. Ky., Lexington, KY USA
SO Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, (1997) Vol. 14, No. 4, pp. A48.
Meeting Info.: National AIDS Malignancy Conference Bethesda, Maryland, USA April 28-30, 1997
ISSN: 1077-9450.
DT **Conference**; Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Enzymes - Physiological Studies *10808
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Virology - Animal Host Viruses *33506

Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Immune System (Chemical Coordination and Homeostasis); Infection; Microbiology; Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; DIDOX; TRIMIDOX; DIDANOSINE
IT Miscellaneous Descriptors
ACQUIRED IMMUNODEFICIENCY SYNDROME; AIDS; ANTIVIRAL-DRUG; BLOOD AND LYMPHATIC DISEASE; DDI; DIDANOSINE; **DIDOX**; ENZYME INHIBITOR-DRUG; IMMUNE SYSTEM DISEASE; INFECTION; LYMPHOMA; MAIDS; MODEL; MURINE ACQUIRED IMMUNODEFICIENCY SYNDROME; NEOPLASTIC DISEASE; PHARMACOLOGY; **RIBONUCLEOTIDE REDUCTASE** INHIBITOR; **RIBONUCLEOTIDE REDUCTASE** INHIBITORS; **TRIMIDOX**; VIRAL DISEASE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
murine (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
69839-83-4 (DIDOX)
95933-74-7 (TRIMIDOX)
69655-05-6 (DIDANOSINE)

L99 ANSWER 4 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:239110 BIOSIS
DN PREV199799538313
TI **Ribonucleotide reductase** inhibitors, **didox** and **trimidox**, demonstrate antiretroviral activity alone or in combination with DDI in a murine acquired immunodeficiency (MAIDS) model.
AU **Elford, H. (1)**; Van't Riet, B. (1); Mayhew, C.; Oakley, O.; Hughes, N.; Piper, J.; Gallicchio, V.
CS (1) Molecules Health Inc., Richmond, VA USA
SO Antiviral Research, (1997) Vol. 34, No. 2, pp. A63.
Meeting Info.: Meeting of the International Society for Antiviral Research and the Tenth International Conference on Antiviral Research Atlanta, Georgia, USA April 6-11, 1997
ISSN: 0166-3542.
DT **Conference**; Abstract; **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Immunology and Immunochemistry - General; Methods *34502
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Muridae *86375

IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis); Infection; Pathology; Pharmacology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; **DIDOX**; **TRIMIDOX**; DIDANOSINE
IT Miscellaneous Descriptors
ACQUIRED IMMUNODEFICIENCY SYNDROME; AIDS; ANTIVIRAL-DRUG; DDI; DIDANOSINE; **DIDOX**; IMMUNE SYSTEM; IMMUNE SYSTEM DISEASE; INFECTION; MAIDS; MODEL; MURINE ACQUIRED IMMUNODEFICIENCY; PHARMACOLOGY; **RIBONUCLEOTIDE REDUCTASE** INHIBITOR; **TRIMIDOX**; VIRAL DISEASE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9040-57-7Q** (**RIBONUCLEOTIDE REDUCTASE**)
9047-64-7Q (**RIBONUCLEOTIDE REDUCTASE**)
9068-66-0Q (**RIBONUCLEOTIDE REDUCTASE**)
69839-83-4 (**DIDOX**)
95933-74-7 (**TRIMIDOX**)
69655-05-6 (DIDANOSINE)

L99 ANSWER 5 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:234222 BIOSIS
DN PREV199799533425
TI Effect of **didox** (3,4-dihydroxybenzohydroxamic acid) and amidox (3,4-dihydroxybenzamidoxime), two new inhibitors of **ribonucleotide reductase** on iron metabolism.
AU Fritzer-Szekeres, M. (1); Vachalkova, A.; Novotny, L.; **Elford, H.**; Szekeres, T.
CS (1) Clin. Inst. Med. Chem., Laboratorydiagnostics, Univ. Vienna, Vienna Austria
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1997) Vol. 38, No. 0, pp. 600.
Meeting Info.: Eighty-eighth Annual Meeting of the American Association for Cancer Research San Diego, California, USA April 12-16, 1997
ISSN: 0197-016X.
DT **Conference**; Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General *10060
Pharmacology - General *22002
Neoplasms and Neoplastic Agents - General *24002
IT Major Concepts
Biochemistry and Molecular Biophysics; Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
DIDOX; **RIBONUCLEOTIDE REDUCTASE**; IRON; 3,4-DIHYDROXYBENZOHYDROXAMIC ACID; AMIDOX
IT Miscellaneous Descriptors
AMIDOX; ANTITUMOR ACTIVITY; DEOXYNUCLEOSIDE TRIPHOSPHATE; **DIDOX**; IRON; METABOLISM; PHARMACOLOGY; **RIBONUCLEOTIDE REDUCTASE** INHIBITOR; SYNTHESIS; TUMOR BIOLOGY; 3,4-DIHYDROXYBENZAMIDOXIME; 3,4-DIHYDROXYBENZOHYDROXAMIC ACID
RN **69839-83-4** (**DIDOX**)

9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
7439-89-6 (IRON)
69839-83-4 (3,4-DIHYDROXYBENZOHYDROXAMIC ACID)
95933-72-5 (AMIDOX)

L99 ANSWER 6 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:232360 BIOSIS
DN PREV199799531563
TI Enhanced effects of adriamycin by combination with a new **ribonucleotide reductase** inhibitor, **trimidox.**
AU Szekeres, T.; Novotny, L.; Romanova, D.; Goebl, R.; Sedlak, J.; Vachalkova, A.; **Elford, H.**
CS Inst. Med. Chemistry, Univ. Vienna, Vienna Austria
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1997) Vol. 38, No. 0, pp. 322.
Meeting Info.: Eighty-eighth Annual Meeting of the American Association for Cancer Research San Diego, California, USA April 12-16, 1997
ISSN: 0197-016X.
DT **Conference;** Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Enzymes - Chemical and Physical *10806
Pathology, General and Miscellaneous - Therapy *12512
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Pharmacology - Blood and Hematopoietic Agents *22008
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
BC Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Pathology; Pharmacology; Tumor Biology
IT Chemicals & Biochemicals
ADRIAMYCIN; **RIBONUCLEOTIDE REDUCTASE; TRIMIDOX**
IT Miscellaneous Descriptors
ADRIAMYCIN; ANTINEOPLASTIC-DRUG; COMBINATION CHEMOTHERAPY; ENZYME INHIBITOR; MOUSE LEUKEMIA CELL; PHARMACOLOGY; POTENTIAL ANTINEOPLASTIC AGENT; **RIBONUCLEOTIDE REDUCTASE; TRIMIDOX** ; TUMOR BIOLOGY
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
L1210 (Muridae): cell line
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN 25316-40-9 (ADRIAMYCIN)
9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
95933-74-7 (TRIMIDOX)

L99 ANSWER 7 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:232359 BIOSIS
DN PREV199799531562
TI **Didox** and **trimidox ribonucleotide reductase** inhibitors exhibit synergistic anticancer activity with doxorubicin, cyclophosphamide or BCNU with protection against doxorubicin cardiac toxicity.
AU **Elford, H. L. (1)**; Van't Riet, B. (1); Novotny, L.; Mikhail, E.; Zweier, J. L.
CS (1) Molecules Health Inc., 800 E. Leigh Street, Richmond, VA 23219 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1997) Vol. 38, No. 0, pp. 322.
Meeting Info.: Eighty-eighth Annual Meeting of the American Association for Cancer Research San Diego, California, USA April 12-16, 1997
ISSN: 0197-016X.
DT **Conference**; Abstract
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Cardiovascular System - Heart Pathology *14506
Pharmacology - General *22002
Toxicology - General; Methods and Experimental *22501
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Muridae *86375
IT Major Concepts
Cardiovascular System (Transport and Circulation); Cell Biology; Pharmacology; Toxicology; Tumor Biology
IT Chemicals & Biochemicals
DIDOX; DOXORUBICIN; CYCLOPHOSPHAMIDE; **TRIMIDOX**
IT Miscellaneous Descriptors
ANTINEOPLASTIC-DRUG; CARDIAC TOXICITY; CYCLOPHOSPHAMIDE; **DIDOX**; DOXORUBICIN; DRUG SYNERGISM; PHARMACOLOGY; **TRIMIDOX**; TUMOR BIOLOGY
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
murine (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **69839-83-4 (DIDOX)**
23214-92-8 (DOXORUBICIN)
50-18-0 (CYCLOPHOSPHAMIDE)
95933-74-7 (TRIMIDOX)

L99 ANSWER 8 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:195971 BIOSIS
DN PREV199799495174
TI In vivo antiretroviral activity of **ribonucleotide reductase** inhibitors hydroxyurea, **didox** and **trimidox** in the HIV-infected model: Mono- and combination therapy.
AU Ussery, M. A. (1); Kunder, S. C. (1); Goldberg, G. (1); Broud, D. D. (1); Hall, B. E. (1); Bacho, M.; Papermaster, S. (1); **Elford, H. L.**; Black, P. L. (1)
CS (1) U.S.F.D.A., Rockville, MD USA
SO Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (1996) Vol. 36, No. 0, pp. 188.
Meeting Info.: 36th ICAAC (International Conference of Antimicrobial

Agents and Chemotherapy) New Orleans, Louisiana, USA September 15-18, 1996
DT **Conference**; Abstract; **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - General *22002
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Retroviridae 02623
Muridae *86375
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Infection; Pathology; Pharmacology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; HYDROXYUREA; **DIDOX**; **TRIMIDOX**; 3,4-DIHYDROXYBENZOHYDROXAMIC ACID
IT Miscellaneous Descriptors
ANIMAL MODEL; ANTIVIRAL-DRUG; **DIDOX**; DRUG COMBINATION THERAPY; DRUG MONOTHERAPY; ENZYME INHIBITOR-DRUG; HUPBMC SCID MOUSE; HYDROXYUREA; INFECTION; PATHOGEN; PHARMACOLOGY; **RIBONUCLEOTIDE REDUCTASE**; SEVERE COMBINED IMMUNODEFICIENCY VIRUS; THERAPEUTIC METHOD; **TRIMIDOX**; 3,4-DIHYDROXYBENZOHYDROXAMIC ACID; 3,4,5-TRIHYDROBENZAMIDOXIME
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Viruses
ORGN Organism Name
human immunodeficiency virus (Retroviridae); HIV (Retroviridae); Muridae (Muridae); Rauscher murine leukemia virus (Retroviridae)
ORGN Organism Superterms
animals; chordates; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates; viruses
RN **9040-57-7Q** (**RIBONUCLEOTIDE REDUCTASE**)
9047-64-7Q (**RIBONUCLEOTIDE REDUCTASE**)
9068-66-0Q (**RIBONUCLEOTIDE REDUCTASE**)
127-07-1 (HYDROXYUREA)
69839-83-4 (**DIDOX**)
95933-74-7 (**TRIMIDOX**)
69839-83-4 (3,4-DIHYDROXYBENZOHYDROXAMIC ACID)

L99 ANSWER 9 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:450886 BIOSIS
DN PREV199699173242
TI Anti-retroviral activity of **ribonucleotide reductase** inhibitors **Didox** and **Trimidox** in a murine acquired immunodeficiency (MAIDS) model either alone or in combination with DDI.
AU Gallicchio, V. S. (1); Mayhew, C.; Oakley, O. R.; Hughes, N. K.; Piper, J.; **Elford, H. L.**
CS (1) Chandler Med. Cent., Univ. Ky., Lexington, KY USA
SO Experimental Hematology (Charlottesville), (1996) Vol. 24, No. 9, pp. 1095.
Meeting Info.: 25th Annual Meeting of the International Society for Experimental Hematology New York, New York, USA August 23-27, 1996
ISSN: 0301-472X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**

Conferences, Congresses, Review Annuals 00520
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology - Blood and Hematopoietic Agents *22008
Immunology and Immunochemistry - Bacterial, Viral and Fungal *34504
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Retroviridae 02623
Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; DIDOX; TRIMIDOX; DIDANOSINE
IT Miscellaneous Descriptors
ANTIVIRAL-DRUG; BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; DDI; DIDANOSINE; **DIDOX;** ENZYME INHIBITOR-DRUG; IMMUNE SYSTEM; INFECTION; MAIDS; MEETING ABSTRACT; MURINE ACQUIRED IMMUNODEFICIENCY; PHARMACOLOGY; **RIBONUCLEOTIDE REDUCTASE; TRIMIDOX;** VIRAL DISEASE
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Viruses
ORGN Organism Name
human immunodeficiency virus (Retroviridae); murine (Muridae); HIV (Retroviridae)
ORGN Organism Superterms
animals; chordates; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates; viruses
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
69839-83-4 (DIDOX)
95933-74-7 (TRIMIDOX)
69655-05-6 (DIDANOSINE)

L99 ANSWER 10 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:399757 BIOSIS
DN PREV199699122113
TI Antiviral activity **ribonucleotide reductase** inhibitors **Didox** and Trimodox in the murine immunodeficiency (MuLV) MAIDS model alone or in combination with DDI.
AU Gallicchio, Vincent S. (1); Mayhew, C.; Oakley, O. Oakley; Hughes, N. K.; Piper, J.; **Elford, H. L.**
CS (1) Markey Cancer Cent., 800 Rose St., Lexington, KY 40536 USA
SO ELEVENTH INTERNATIONAL CONFERENCE ON AIDS.. (1996) pp. 59. Eleventh International Conference on AIDS, Vol. Two. One world: One hope.
Publisher: Eleventh International Conference on AIDS Vancouver, British Columbia, Canada.
Meeting Info.: Eleventh International Conference on AIDS, Vol. Two. One world: One hope Vancouver, British Columbia, Canada July 7-12, 1996
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of**

Conferences, Congresses, Review Annuals 00520
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Pathology, General and Miscellaneous - Therapy *12512
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Immunological Processes and Allergy *22018
Virology - Animal Host Viruses 33506
Immunology and Immunochemistry - Bacterial, Viral and Fungal *34504
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Medical and Clinical Microbiology - Virology *36006

BC Retroviridae 02623
Hominidae 86215
Muridae *86375

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Infection; Pathology; Pharmacology

IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; DIDOX; DIDANOSINE

IT Miscellaneous Descriptors
ACQUIRED IMMUNODEFICIENCY SYNDROME; ANTIVIRAL-DRUG; DIDANOSINE; HUMAN MODEL; MEETING ABSTRACT; MEETING POSTER

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Viruses

ORGN Organism Name
human immunodeficiency virus (Retroviridae); Hominidae (Hominidae); Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; humans; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates; viruses

RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
69839-83-4 (DIDOX)
69655-05-6 (DIDANOSINE)

L99 ANSWER 11 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:256551 BIOSIS
DN PREV199698812680
TI Effect of **trimidox** (3,4,5-trihydroxybenzamidoxime), a new inhibitor of **ribonucleotide reductase** on iron metabolism.
AU Fritzer-Szekeres, M. (1); Vielnascher, E.; Novotny, L.; Vachalkova, A.; Findenig, G.; Goebl, R.; **Elford, H. L.**; Goldenberg, H.; Szekeres, T.
CS (1) Clin. Inst. Med. Chem. Laboratorydiagnostics, Univ. Vienna Med. Sch., Vienna Austria
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 359.
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996
ISSN: 0197-016X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**

Cytology and Cytochemistry - Human *02508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Minerals 10069
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Minerals *13010
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Blood and Hematopoietic Agents *22008
Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
In Vitro Studies, Cellular and Subcellular *32600

BC Hominidae *86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Enzymology (Biochemistry and Molecular Biophysics); Hematology (Human Medicine, Medical Sciences); Membranes (Cell Biology); Metabolism; Oncology (Human Medicine, Medical Sciences); Pathology; Pharmacology; Skeletal System (Movement and Support)

IT Chemicals & Biochemicals
TRIMIDOX; RIBONUCLEOTIDE REDUCTASE; IRON; TRIPHOSPHATE

IT Miscellaneous Descriptors
ANTINEOPLASTIC-DRUG; CANCER BIOCHEMISTRY; CANCER CHEMOTHERAPY; DEOXYNUCLEOSIDE TRIPHOSPHATE SYNTHESIS; ENZYME INHIBITOR-DRUG; EXPERIMENTAL CANCER THERAPEUTICS; HEMATOLOGIC-DRUG; HL-60 PROMYELOCYTIC LEUKEMIA CELL LINE; IN-VITRO; IN-VIVO; MEETING ABSTRACT; MOLECULAR MECHANISM; PHARMACODYNAMICS; PHARMACOKINETICS; TRANSFERRIN RECEPTOR;
TRIMIDOX; 3,4,5-TRIHYDROXYBENZAMIDOXIME

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN **95933-74-7 (TRIMIDOX)**
9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
7439-89-6 (IRON)
14127-68-5 (TRIPHOSPHATE)

L99 ANSWER 12 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:256104 BIOSIS
DN PREV199698812233
TI **Ribonucleotide reductase** inhibitors **Didox** and **Trimidox** enhance antitumor activity of Anthracyclines, Cytoxan and Pt compounds and protect against Anthracycline cardiac toxicity.
AU **Elford, H. L. (1)**; Van't Riet, B. (1); Novotny, L.; Mikhail, E.; Zweier, J. L.
CS (1) Molecules Health Inc., 3313 Gloucester Rd., Richmond, VA 23227 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 294.
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996
ISSN: 0197-016X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Minerals 10069
Enzymes - Physiological Studies *10808
Cardiovascular System - Heart Pathology *14506
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology - Blood and Hematopoietic Agents *22008
Toxicology - Pharmacological Toxicology *22504
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
BC Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular System (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Pharmacology; Toxicology; Tumor Biology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; DIDOX; TRIMIDOX; CYTOXAN; CISPLATIN; ADRIAMYCIN
IT Miscellaneous Descriptors
ADRIAMYCIN; ANTINEOPLASTIC-DRUG; CISPLATIN; CYTOXAN; **DIDOX**; ENZYME INHIBITOR-DRUG; L1210 LEUKEMIA; MEETING ABSTRACT; MEETING POSTER; **TRIMIDOX**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
69839-83-4 (DIDOX)
95933-74-7 (TRIMIDOX)
50-18-0 (CYTOXAN)
15663-27-1 (CISPLATIN)

25316-40-9 (ADRIAMYCIN)

L99 ANSWER 13 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:212315 BIOSIS
DN PREV199698768444
TI Antiretroviral activity of **ribonucleotide reductase** inhibitors hydroxyurea, **didox** and **trimidox** in the in vivo Rauscher murine leukemia virus (RMuLV) model: Mono- and combination therapy.
AU Kunder, Steven C. (1); Black, Paul L. (1); Hall, Bradford E. (1); **Elford, Howard L.**; Ussery, Michael A. (1)
CS (1) U.S.F.D.A., Rockville, MD USA
SO INFECTIOUS DISEASES SOCIETY OF AMERICA; NATIONAL INSTITUTES OF HEALTH; CENTERS FOR DISEASE CONTROL AND PREVENTION.. (1996) pp. 117. 3rd Conference on retroviruses and opportunistic infections.
Publisher: Infectious Diseases Society of America for the Foundation for Retrovirology and Human Health Suite 104, 11 Canal Center Plaza, Alexandria, Virginia 22314, USA.
Meeting Info.: Meeting Washington, DC, USA January 28-February 2, 1996
ISBN: 1-888700-00-9.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Enzymes - Physiological Studies *10808
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Genetics of Bacteria and Viruses *31500
Virology - Animal Host Viruses 33506
Immunology and Immunochemistry - Bacterial, Viral and Fungal *34504
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Retroviridae 02623
Muridae *86375
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Enzymology (Biochemistry and Molecular Biophysics); Genetics; Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology
IT Chemicals & Biochemicals
RIBONUCLEOTIDE REDUCTASE; HYDROXYUREA; **DIDOX**; **TRIMIDOX**
IT Miscellaneous Descriptors
ANTIVIRAL-DRUG; **DIDOX**; HYDROXYUREA; MEETING ABSTRACT; MEETING POSTER; **TRIMIDOX**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae: Viruses
ORGN Organism Name
human immunodeficiency virus (Retroviridae); Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates; viruses
RN **9040-57-7Q (RIBONUCLEOTIDE REDUCTASE)**
9047-64-7Q (RIBONUCLEOTIDE REDUCTASE)
9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)
127-07-1 (HYDROXYUREA)

69839-83-4 (DIDOX)
95933-74-7 (TRIMIDOX)

L99 ANSWER 14 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1994:289742 BIOSIS
DN PREV199497302742
TI Synergistic cytotoxic and differentiating effects a new inhibitor of **ribonucleotide reductase** (**trimidox**) with tiazofurin in HL-60 cells.
AU Szekeres, T. (1); Fritzer, M. (1); Strobl, H.; **Elford, H.**; Gharehbaghi, K.; Jayaram, H. N.
CS (1) Inst. Med. Chem., Univ. Vienna, Vienna Austria
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 330.
Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 10-13, 1994
ISSN: 0197-016X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Pharmacology - Clinical Pharmacology *22005
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Hominidae *86215
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Oncology (Human Medicine, Medical Sciences); Pharmacology
IT Chemicals & Biochemicals
REDUCTASE; TIAZOFURIN; **TRIMIDOX**
IT Miscellaneous Descriptors
ANTINEOPLASTIC-DRUG; DRUG-DRUG INTERACTION; EXPERIMENTAL THERAPEUTICS; MEETING ABSTRACT; TIAZOFURIN; **TRIMIDOX**
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 9037-80-3 (REDUCTASE)
60084-10-8 (TIAZOFURIN)
95933-74-7 (TRIMIDOX)

L99 ANSWER 15 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1994:289710 BIOSIS
DN PREV199497302710
TI **Didox**: A **ribonucleotide reductase** inhibitor anticancer drug that enhances antitumor activity and ameliorates the toxicity of adriamycin.
AU **Elford, H. L.**; Van't Riet, B.
CS Molecules Health Inc., 3313 Gloucester Road, Richmond, VA 23227 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 324.
Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 10-13, 1994
ISSN: 0197-016X.

DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Toxicology - Pharmacological Toxicology *22504
Toxicology - Antidotes and Preventative Toxicology *22505
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Rodentia - Unspecified *86265
IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Toxicology; Tumor Biology
IT Chemicals & Biochemicals
DIDOX; REDUCTASE; ADRIAMYCIN
IT Miscellaneous Descriptors
ADRIAMYCIN; ANTIDOTE-DRUG; ANTINEOPLASTIC-DRUG; **DIDOX** A; ENZYME INHIBITOR-DRUG; EXPERIMENTAL THERAPEUTICS; MEETING ABSTRACT; PHARMACEUTICAL ADJUNCT-DRUG
ORGN Super Taxa
Rodentia - Unspecified: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
rodent (Rodentia - Unspecified); Rodentia (Rodentia - Unspecified)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
RN **69839-83-4 (DIDOX)**
9037-80-3 (REDUCTASE)
23214-92-8Q (ADRIAMYCIN)
25316-40-9Q (ADRIAMYCIN)

L99 ANSWER 16 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:400153 BIOSIS
DN PREV199345058978
TI **Trimidox**: A new member of the polyhydroxyphenyl series of compounds that inhibit **ribonucleotide reductase** and possess antitumor activity.
AU **Elford, H. L. (1)**; Wampler, G. L.; Van't Riet, B. (1)
CS (1) Molecules Health Inc., Richmond, VA 23227 USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1993) Vol. 34, No. 0, pp. 382.
Meeting Info.: 84th Annual Meeting of the American Association for Cancer Research Orlando, Florida, USA May 19-22, 1993
ISSN: 0197-016X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Pathology, General and Miscellaneous - Therapy 12512
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology - Clinical Pharmacology 22005
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Tumor Biology
IT Chemicals & Biochemicals
TRIMIDOX; REDUCTASE; HYDROCHLORIC ACID; **DIDOX**; 3 4-DIHYDROXYBENZOHYDROXAMIC ACID
IT Miscellaneous Descriptors
ABSTRACT; ANTINEOPLASTIC-DRUG; **DIDOX**; LEUKEMIA; N-3 4 5=TETRAHYDROXYBENZIMIDAMIDE HYDROCHLORIC ACID; 3 4=DIHYDROXYBENZOHYDROXAMIC ACID
RN **95933-74-7 (TRIMIDOX)**
9037-80-3 (REDUCTASE)
7647-01-0 (HYDROCHLORIC ACID)
69839-83-4 (DIDOX)
69839-83-4 (3 4-DIHYDROXYBENZOHYDROXAMIC ACID)

L99 ANSWER 17 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:379092 BIOSIS
DN PREV199345050517
TI Cytotoxic effects of a new inhibitor of **ribonucleotide reductase**.
AU Szekeres, T. (1); Fritzer, M. (1); **Elford, H.**; Gharehbaghi, K.; Jayaram, H. N.
CS (1) Inst. Med. Chem., Univ. Vienna Austria
SO Proceedings of the American Association for Cancer Research Annual Meeting, (1993) Vol. 34, No. 0, pp. 296.
Meeting Info.: 84th Annual Meeting of the American Association for Cancer Research Orlando, Florida, USA May 19-22, 1993
ISSN: 0197-016X.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Chemical and Physical *10806
Pathology, General and Miscellaneous - Therapy 12512
Digestive System - Pathology *14006
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Enzymology (Biochemistry and Molecular Biophysics); Tumor Biology
IT Chemicals & Biochemicals
REDUCTASE; **TRIMIDOX**
IT Miscellaneous Descriptors
ABSTRACT; ANTINEOPLASTIC-DRUG; COLON CARCINOMA; LEUKEMIA; **TRIMIDOX**; 3 4 5=TRIHYDROXYBENZAMIDAMINE
RN 9037-80-3 (REDUCTASE)
95933-74-7 (TRIMIDOX)

L99 ANSWER 18 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1992:403529 BIOSIS
DN BR43:59404
TI **DIDOX** EXHIBITS ANTIVIRAL ACTIVITY IN A RETROVIRUS ANIMAL MODEL.
AU MILLS D L; **ELFORD H L**; RIET B V; WEBB S R
CS BIOL. DEP., VIRGINIA COMMONWEALTH UNIV., VA. 23284.
SO 83RD ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, SAN DIEGO, CALIFORNIA, USA, MAY 20-23, 1992. PROC AM ASSOC CANCER RES ANNU MEET. (1992) 33 (0), 399.
CODEN: PAMREA.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy *12512
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology 22005
Pharmacology - Blood and Hematopoietic Agents *22008
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
Genetics of Bacteria and Viruses *31500
Medical and Clinical Microbiology - Virology *36006
Chemotherapy - Antiviral Agents *38506
BC Retroviridae - Oncovirinae 02244
Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT MOUSE FRIEND LEUKEMIA VIRUS ANTINEOPLASTIC-DRUG ENZYME INHIBITOR-DRUG ANTIVIRAL-DRUG **RIBONUCLEOTIDE REDUCTASE** INHIBITION CARCINOGENESIS
RN **69839-83-4 (DIDOX)**
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

L99 ANSWER 19 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1991:353632 BIOSIS
DN BR41:38147
TI STUDIES ON THE MECHANISMS OF INHIBITION OF L1210 CELL GROWTH BY 3 4 DIHYDROXYBENZOHYDROXAMIC ACID AND 3 4 DIHYDROXYBENZAMIDOXIME.
AU TIHAN T; **ELFORD H L**; CORY J G
CS DEP. BIOCHEM., BRODY MED. SCI. BUILD., EAST CAROLINA UNIV. SCH. MED., GREENVILLE, N.C. 27858, USA.
SO WEBER, G. (ED.). ADVANCES IN ENZYME REGULATION, VOL. 31; SYMPOSIUM ON REGULATION OF ENZYME ACTIVITY AND SYNTHESIS IN NORMAL AND NEOPLASTIC TISSUES, INDIANAPOLIS, INDIANA, USA, OCTOBER 1-2, 1990. XVI+496P. PERGAMON PRESS: OXFORD, ENGLAND, UK; ELMSFORD, NEW YORK, USA. ILLUS. (1991) 0 (0), 71-84.
CODEN: AEZRA2. ISSN: 0065-2571. ISBN: 0-08-041142-8.
DT **Conference**
FS BR; OLD
LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Chemical and Physical *10806
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Tissue Culture, Apparatus, Methods and Media 32500
BC Muridae 86375
IT Miscellaneous Descriptors
MOUSE AMIDOX **DIDOX** ANTINEOPLASTIC-DRUG ENZYME INHIBITOR-DRUG **RIBONUCLEOTIDE REDUCTASE** PHARMACODYNAMICS
RN **69839-83-4** (3 4 DIHYDROXYBENZOHYDROXAMIC ACID)
69839-83-4 (DIDOX)
95933-72-5 (AMIDOX)
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

L99 ANSWER 20 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1990:326250 BIOSIS
DN BR39:33586
TI PHASE I CLINICAL TRIALS OF **DIDOX.**
AU CARMICHAEL J; CANTWELL B M J; MANNIX K A; VEALE D; **ELFORD H L;** VAN'T RIET B; BLACKIE R; KERR D J; KAYE S B; HARRIS A L
CS CHURCHILL HOSP., HEADINGTON, OXFORD, UK.
SO 81ST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, WASHINGTON, D.C., USA, MAY 23-26, 1990. PROC AM ASSOC CANCER RES ANNU MEET. (1990) 31 (0), 177.
CODEN: PAMREA.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Pharmacology - Clinical Pharmacology *22005
Toxicology - Pharmacological Toxicology *22504
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Hominidae 86215
IT Miscellaneous Descriptors
ABSTRACT HUMAN ANTINEOPLASTIC-DRUG **RIBONUCLEOTIDE REDUCTASE** INHIBITOR TOXICITY
RN **69839-83-4 (DIDOX)**
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

L99 ANSWER 21 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1990:125680 BIOSIS
DN BR38:59890
TI SYNERGISTIC POTENTIAL AND INITIAL PHASE I RESULTS OF THE NEW **RIBONUCLEOTIDE REDUCTASE** INHIBITOR 3 4 DIHYDROXYBENZOHYDROXAMIC ACID **DIDOX.**

AU CARMICHAEL J; CANTWELL B M J; VEALE D; HARRIS A L; **ELFORD H L**; VAN'T RIET B; BLACKIE R; KERR D J; KAYE S B
CS UNIV. NEWCASTLE UPON TYNE, UNITED KINGDOM.
SO SIXTH NCI-EORTC (NATIONAL CANCER INSTITUTE-EUROPEAN ORGANIZATION FOR RESEARCH ON TREATMENT OF CANCER) SYMPOSIUM ON NEW DRUGS IN CANCER THERAPY, AMSTERDAM, NETHERLANDS, MARCH 7-10, 1989. INVEST NEW DRUGS. (1989) 7 (4), 381.
CODEN: INNDDK. ISSN: 0167-6997.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Pharmacology - General *22002
Pharmacology - Drug Metabolism; Metabolic Stimulators 22003
Pharmacology - Clinical Pharmacology *22005
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
BC Hominidae 86215
IT Miscellaneous Descriptors
ABSTRACT HUMAN METASTATIC CARCINOMA DOXORUBICIN CYCLOPHOSPHAMIDE 1 3 BIS-2-CHLOROETHYL-1-NITROSOUREA ANTINEOPLASTIC-DRUG
RN 50-18-0 (CYCLOPHOSPHAMIDE)
154-93-8 (1 3 BIS-2-CHLOROETHYL-1-NITROSOUREA)
23214-92-8 (DOXORUBICIN)
69839-83-4 (DIDOX)
69839-83-4 (3 4 DIHYDROXYBENZOHYDROXAMIC ACID)
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (**RIBONUCLEOTIDE REDUCTASE**)

L99 ANSWER 22 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1988:365193 BIOSIS
DN BR35:49806
TI **DIDOX** A NEW ANTICANCER DRUG THAT INHIBITS **RIBONUCLEOTIDE REDUCTASE** PROTECTS AGAINST TOXICITY AND POTENTIATES ANTITUMOR ACTIVITY OF ANTHRACYCLINES.
AU **ELFORD H**; VAN'T RIET B; HERMAN E
CS MOLECULES HEALTH INC., 3313 GLOUCESTER, RICHMOND, VA. 23227.
SO HACKER, M. P., J. S. LAZO AND T. R. TRITTON (ED.). DEVELOPMENTS IN ONCOLOGY: ORGAN DIRECTED TOXICITIES OF ANTICANCER DRUGS; FIRST INTERNATIONAL SYMPOSIUM, BURLINGTON, VERMONT, USA, JUNE 4-6, 1987. XII+254P. KLUWER ACADEMIC PUBLISHERS: DORDRECHT, NETHERLANDS; BOSTON, MASSACHUSETTS, USA. ILLUS. (1988) 0 (0), 221.
CODEN: DEOND5. ISSN: 0167-4927. ISBN: 0-89838-356-0.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006

Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Respiratory System - Pathology *16006
Pharmacology - Drug Metabolism; Metabolic Stimulators 22003
Pharmacology - Blood and Hematopoietic Agents *22008
Pharmacology - Respiratory System *22030
Toxicology - Pharmacological Toxicology *22504
Toxicology - Antidotes and Preventative Toxicology *22505
Neoplasms and Neoplastic Agents - Biochemistry *24006
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010

BC Muridae 86375

IT Miscellaneous Descriptors
ABSTRACT MOUSE LEWIS LUNG TUMOR L1210 LEUKEMIA DOXORUBICIN ANTINEOPLASTIC-DRUG ANTIDOTE-DRUG

RN 23214-92-8 (DOXORUBICIN)
69839-83-4 (DIDOX)
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

L99 ANSWER 23 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1988:344245 BIOSIS
DN BR35:39087
TI PHASE I STUDY OF **DIDOX** A NEW INHIBITOR OF **RIBONUCLEOTIDE REDUCTASE**.
AU VEALE D; CARMICHAEL J; CANTWELL B M J; **ELFORD H L**; VAN'T RIET B; KAYE S B; HARRIS A L
CS FREEMAN HOSP., NEWCASTLE-UPON-TYNE NE4 6BE, ENGLAND.
SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET. (1988) 29 (0), 219.
CODEN: PAMREA.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - General 10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Therapy 12512
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology *22005
Toxicology - Pharmacological Toxicology *22504
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

BC Hominidae 86215

IT Miscellaneous Descriptors
ABSTRACT HUMAN 3 4 DIHYDROXYBENZOHYDROXAMIC ACID ANTINEOPLASTIC-DRUG TOXICITY

RN **69839-83-4 (DIDOX)**
69839-83-4 (3 4 DIHYDROXYBENZOHYDROXAMIC ACID)
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

L99 ANSWER 24 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1988:299431 BIOSIS
DN BR35:16255
TI SYNERGISTIC POTENTIAL OF NEW **RIBONUCLEOTIDE REDUCTASE**

INHIBITOR 3 4 DIHYDROXYBENZOHYDROXAMIC ACID **DIDOX** WITH DNA INTERACTING ANTI-CANCER COMPOUNDS.

AU **ELFORD H L;** VAN'T RIET B

CS MOL. HEALTH, INC., 3313 GLOUCESTER RD., RICHMOND, VA. 23227.

SO 72ND ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, LAS VEGAS, NEVADA, USA, MAY 1-5, 1988. FASEB (FED AM SOC EXP BIOL) J. (1988) 2 (5), ABSTRACT 6118.
CODEN: FAJOEC. ISSN: 0892-6638.

DT **Conference**

FS BR; OLD

LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Human 02508
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Toxicology - Pharmacological Toxicology *22504
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
In Vitro Studies, Cellular and Subcellular 32600

BC Vertebrata - Unspecified 85150
Hominidae 86215

IT Miscellaneous Descriptors
ABSTRACT ANIMAL HUMAN ANTINEOPLASTIC-DRUG ANTHRACYCLINE TOXICITY

RN **9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)**

L99 ANSWER 25 OF 25 BIOSIS COPYRIGHT 1999 BIOSIS

AN 1987:370957 BIOSIS

DN BR33:61432

TI **DIDOX** A NEW ANTICANCER DRUG THAT INHIBITS **RIBONUCLEOTIDE REDUCTASE** PROGRESS REPORT.

AU **ELFORD H;** SMITH F; SOINE W; VAN'T RIET B

CS MOLECULES HEALTH INC., RICHMOND, VA 23227, USA.

SO SEVENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ATLANTA, GEORGIA, USA, MAY 20-23, 1987. PROC AM ASSOC CANCER RES ANNU MEET. (1987) 28 (0), 417.
CODEN: PAMREA.

DT **Conference**

FS BR; OLD

LA English

CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates 10068
Enzymes - Chemical and Physical *10806
Pathology, General and Miscellaneous - Therapy 12512
Metabolism - General Metabolism; Metabolic Pathways 13002
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Respiratory System - Pathology *16006
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

Pharmacology - Clinical Pharmacology 22005
Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
Neoplasms and Neoplastic Agents - Blood and Reticuloendothelial Neoplasms *24010
BC Hominidae 86215
Muridae 86375
IT Miscellaneous Descriptors
ABSTRACT HUMAN MOUSE LEUKEMIA L1210 CELL RAT LEWIS LUNG TUMOR ENZYME INHIBITOR-DRUG DOXORUBICIN CYCLOPHOSPHAMIDE ETOPOSIDE BLEOMYCIN 1 3 BIS-2-CHLOROETHYL-1-NITROSOUREA ANTINEOPLASTIC-DRUG PHARMACOKINETICS DRUG-DRUG SYNERGY
RN 50-18-0 (CYCLOPHOSPHAMIDE)
154-93-8 (1 3 BIS-2-CHLOROETHYL-1-NITROSOUREA)
11056-06-7 (BLEOMYCIN)
23214-92-8 (DOXORUBICIN)
33419-42-0 (ETOPOSIDE)
69839-83-4 (DIDOX)
9040-57-7Q, 9047-64-7Q, 9068-66-0Q (RIBONUCLEOTIDE REDUCTASE)

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=> d his l100-

     (FILE 'BIOSIS' ENTERED AT 15:03:31 ON 30 MAR 1999)

     FILE 'EMBASE' ENTERED AT 15:04:22 ON 30 MAR 1999
L100          45 S L88
L101          33 S L62
L102          30 S "3,4 DIHYDROXYBENZOHYDROXAMIC ACID"/CT
L103           0 S 95933-74-7
L104           3 S 69839-82-3
L105           6 S "3,4,5 TRIHYDROXYBENZOHYDROXAMIC ACID"/CT
L106          35 S L101,L102,L104,L105
L107          12 S L100 NOT L106
L108           8 S "3,4,5 TRIHYDROXYBENZOHYDROXAMIDOXIME"/CT
L109          47 S L100,L106,L108
L110        4303 S L31
L111           1 S L109 AND L110
L112           1 S TRANSCRIPTION FACTOR?/CT AND L109
L113           1 S L111,L112

=> d all

L113 ANSWER 1 OF 1  EMBASE  COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN   97259546  EMBASE
DN   1997259546
TI   Selective inhibition of I.kappa.B.alpha. phosphorylation and HIV-1
     LTR-directed gene expression by novel antioxidant compounds.
AU   Lee R.; Beauparlant P.; Elford H.; Ponka P.; Hiscott J.
CS   J. Hiscott, Lady Davis Inst. for Med. Research, 3755 Cote Ste. Catherine,
     Montreal, Que. H3T1E2, Canada. mijh@musica.mcgill.ca
SO   Virology, (1997) 234/2 (277-290).
     Refs: 72
     ISSN: 0042-6822  CODEN: VIRLAX
CY   United States
DT   Journal; Article
FS   004     Microbiology
     037     Drug Literature Index
LA   English
SL   English
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Ang.

QR1 .V5

AB Oxidative stress activates the **NF-.kappa.**B/Rel transcription factors which are involved in the activation of numerous immunoregulatory genes and the human immunodeficiency virus type 1 (HIV-1) long terminal repeat (LTR). In the present study, we examined the effects of established and never compounds including antioxidants, ribonucleotide reductase inhibitors, and iron chelators on **NF-.kappa**.B activation and HIV LTR-mediated gene expression induced by TNF-.alpha.. N-Acetylcysteine (NAC), pyrrolidinedithiocarbamate (PDTC), and **Trimidox** (TD) at various concentrations inhibited TNF-.alpha.-induced **NF-.kappa.**B binding in Jurkat cells. Pretreatment of cells with these compounds odor to stimulation prevented I.kappa.B.alpha. degradation. Phosphorylation of I.kappa.B.alpha., a prerequisite for its signal-induced degradation, was abrogated in these cells, indicating that oxidative stress is an essential step in the **NF-.kappa.**B activation pathway. On the other hand, iron chelators desferrioxamine, pyridoxal isonicotinoyl hydrazone (PIH), and salicylaldehyde isonicotinoyl hydrazone (SIH) snowed no inhibition of TNF-.alpha.-induced **NF-.kappa.**B DNA-binding activity. Synergistic induction of HIV-1 LTR-mediated gene expression by TNF- .alpha. and the HIV-1 transactivator Tat in Jurkat cells was significantly suppressed in the presence of NAC and TD, but not PDTC. The inhibition of NAC and TD on LTR-directed gene expression was diminished when **NF-.kappa.**B-binding sites in the LTR were deleted, indicating that these compounds affected the **NF-.kappa.**B component of the synergism. Iron chelators PIH and SIH also snowed some inhibitory effect on LTR-mediated gene activation, presumably through an **NF-.kappa.**B-independent mechanism. These experiments demonstrate that TD, at concentration 50 times lower than the effective concentration of NAC, potently inhibits **NF-.kappa.**B activity and suppresses HIV LTR expression.

CT Medical Descriptors:
*antioxidant activity
*human immunodeficiency virus 1
*long terminal repeat
*virus inhibition
article
controlled study
enzyme inhibition
gene activation
gene expression regulation
human
human cell
leukemia cell line
nonhuman
oxidative stress
priority journal
protein phosphorylation
Drug Descriptors:
***3,4 dihydroxybenzohydroxamic acid: AN, drug analysis**
***3,4 dihydroxybenzohydroxamic acid: CM, drug comparison**
*acetylcysteine: AN, drug analysis
*acetylcysteine: CM, drug comparison
*amidox: AN, drug analysis
*amidox: CM, drug comparison
*antioxidant: AN, drug analysis
*antioxidant: CM, drug comparison
*immunoglobulin enhancer binding protein
chelating agent: AN, drug analysis
chelating agent: CM, drug comparison

deferoxamine: CM, drug comparison
deferoxamine: AN, drug analysis
dithiocarbamic acid derivative: AN, drug analysis
dithiocarbamic acid derivative: CM, drug comparison
pyridoxal isonicotinoylhydrazone: AN, drug analysis
pyridoxal isonicotinoylhydrazone: CM, drug comparison
pyrrolidine derivative: AN, drug analysis
pyrrolidine derivative: CM, drug comparison
salicylaldehyde: AN, drug analysis
salicylaldehyde: CM, drug comparison
transcription factor
tumor necrosis factor alpha
RN (3,4 dihydroxybenzohydroxamic acid) **69839-83-4**; (acetylcysteine) 616-91-1; (amidox) 95933-72-5; (deferoxamine) 70-51-9; (pyridoxal isonicotinoylhydrazone) 737-86-0; (salicylaldehyde) 90-02-8